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NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

Abstract:

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## NOVEL NUCLEIC ACIDS AND POLYPEPTIDES

### 1. TECHNICAL FIELD

The present invention provides novel polynucleotides and proteins encoded by such polynucleotides, along with uses for these polynucleotides and proteins, for example in therapeutic, diagnostic and research methods.

### 2. BACKGROUND

Technology aimed at the discovery of protein factors (including *e.g.*, cytokines, such as lymphokines, interferons, circulating soluble factors, chemokines, and interleukins) has matured rapidly over the past decade. The now routine hybridization cloning and expression cloning techniques clone novel polynucleotides "directly" in the sense that they rely on information directly related to the discovered protein (*i.e.*, partial DNA/amino acid sequence of the protein in the case of hybridization cloning; activity of the protein in the case of expression cloning). More recent "indirect" cloning techniques such as signal sequence cloning, which isolates DNA sequences based on the presence of a now well-recognized secretory leader sequence motif, as well as various PCR-based or low stringency hybridization-based cloning techniques, have advanced the state of the art by making available large numbers of DNA/amino acid sequences for proteins that are known to have biological activity, for example, by virtue of their secreted nature in the case of leader sequence cloning, by virtue of their cell or tissue source in the case of PCR-based techniques, or by virtue of structural similarity to other genes of known biological activity.

Identified polynucleotide and polypeptide sequences have numerous applications in, for example, diagnostics, forensics, gene mapping; identification of mutations responsible for genetic disorders or other traits, to assess biodiversity, and to produce many other types of data and products dependent on DNA and amino acid sequences.

### 3. SUMMARY OF THE INVENTION

The compositions of the present invention include novel isolated polypeptides, novel isolated polynucleotides encoding such polypeptides, including recombinant DNA molecules, cloned genes or degenerate variants thereof, especially naturally occurring variants such as allelic variants, antisense polynucleotide molecules, and antibodies that specifically recognize one or more epitopes present on such polypeptides, as well as hybridomas producing such antibodies.

The compositions of the present invention additionally include vectors, including expression vectors, containing the polynucleotides of the invention, cells genetically engineered to contain such polynucleotides and cells genetically engineered to express such polynucleotides.

The present invention relates to a collection or library of at least one novel nucleic acid sequence assembled from expressed sequence tags (ESTs) isolated mainly by sequencing by hybridization (SBH), and in some cases, sequences obtained from one or more public databases. The invention relates also to the proteins encoded by such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins. These nucleic acid sequences are designated as SEQ ID NO: 1-5497. The polypeptides sequences are designated SEQ ID NO: 5498-10994. The nucleic acids and polypeptides are provided in the Sequence Listing. In the nucleic acids provided in the Sequence Listing, A is adenosine; C is cytosine; G is guanine; T is thymine; and N is any of the four bases. In the amino acids provided in the Sequence Listing, \* corresponds to the stop codon.

The nucleic acid sequences of the present invention also include, nucleic acid sequences that hybridize to the complement of SEQ ID NO: 1-5497 under stringent hybridization conditions; nucleic acid sequences which are allelic variants or species homologues of any of the nucleic acid sequences recited above, or nucleic acid sequences that encode a peptide comprising a specific domain or truncation of the peptides encoded by SEQ ID NO: 1-5497. A polynucleotide comprising a nucleotide sequence having at least 90% identity to an identifying sequence of SEQ ID NO: 1-5497 or a degenerate variant or fragment thereof. The identifying sequence can be 100 base pairs in length.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-5497. The sequence information can be a segment of any one of SEQ ID NO: 1-5497 that uniquely identifies or represents the sequence information of SEQ ID NO: 1-5497.

A collection as used in this application can be a collection of only one polynucleotide. The collection of sequence information or identifying information of each sequence can be provided on a nucleic acid array. In one embodiment, segments of sequence information is provided on a nucleic acid array to detect the polynucleotide that contains the segment. The array can be designed to detect full-match or mismatch to the polynucleotide that contains the segment. The collection can also be provided in a computer-readable format.

This invention also includes the reverse or direct complement of any of the nucleic acid sequences recited above; cloning or expression vectors containing the nucleic acid sequences; and host cells or organisms transformed with these expression vectors. Nucleic acid sequences (or their reverse or direct complements) according to the invention have numerous applications in a variety



of techniques known to those skilled in the art of molecular biology, such as use as hybridization probes, use as primers for PCR, use in an array, use in computer-readable media, use in sequencing full-length genes, use for chromosome and gene mapping, use in the recombinant production of protein, and use in the generation of anti-sense DNA or RNA, their chemical analogs and the like.

5 In a preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-5497 or novel segments or parts of the nucleic acids of the invention are used as primers in expression assays that are well known in the art. In a particularly preferred embodiment, the nucleic acid sequences of SEQ ID NO: 1-5497 or novel segments or parts of the nucleic acids provided herein are used in diagnostics for identifying expressed genes or, as well known in the art and exemplified by Vollrath  
10 et al., *Science* 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The isolated polynucleotides of the invention include, but are not limited to, a polynucleotide comprising any one of the nucleotide sequences set forth in SEQ ID NO: 1-5497; a polynucleotide comprising any of the full length protein coding sequences of SEQ ID NO: 1-5497;  
15 and a polynucleotide comprising any of the nucleotide sequences of the mature protein coding sequences of SEQ ID NO: 1-5497. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent hybridization conditions to (a) the complement of any one of the nucleotide sequences set forth in SEQ ID NO: 1-5497; (b) a nucleotide sequence encoding any one of the amino acid sequences set forth in the Sequence Listing  
20 (*e.g.*, SEQ ID NO: 5498-10994); (c) a polynucleotide which is an allelic variant of any polynucleotides recited above; (d) a polynucleotide which encodes a species homolog (*e.g.* orthologs) of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of any of the polypeptides comprising an amino acid sequence set forth in the Sequence Listing.

25 The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising any of the amino acid sequences set forth in the Sequence Listing; or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides with biological activity that are encoded by (a) any of the polynucleotides having a nucleotide sequence set forth in SEQ ID NO: 1-5497; or (b) polynucleotides that hybridize to the complement of the  
30 polynucleotides of (a) under stringent hybridization conditions. Biologically or immunologically active variants of any of the polypeptide sequences in the Sequence Listing, and "substantial equivalents" thereof (*e.g.*, with at least about 65%, 70%, 75%, 80%, 85%, 90%, 95%, 98% or 99% amino acid sequence identity) that preferably retain biological activity are also contemplated. The polypeptides of the invention may be wholly or partially chemically synthesized but are preferably

produced by recombinant means using the genetically engineered cells (e.g. host cells) of the invention.

The invention also provides compositions comprising a polypeptide of the invention. Polypeptide compositions of the invention may further comprise an acceptable carrier, such as a hydrophilic, e.g., pharmaceutically acceptable, carrier.

The invention also provides host cells transformed or transfected with a polynucleotide of the invention.

The invention also relates to methods for producing a polypeptide of the invention comprising growing a culture of the host cells of the invention in a suitable culture medium under conditions permitting expression of the desired polypeptide, and purifying the polypeptide from the culture or from the host cells. Preferred embodiments include those in which the protein produced by such process is a mature form of the protein.

Polynucleotides according to the invention have numerous applications in a variety of techniques known to those skilled in the art of molecular biology. These techniques include use as hybridization probes, use as oligomers, or primers, for PCR, use for chromosome and gene mapping, use in the recombinant production of protein, and use in generation of anti-sense DNA or RNA, their chemical analogs and the like. For example, when the expression of an mRNA is largely restricted to a particular cell or tissue type, polynucleotides of the invention can be used as hybridization probes to detect the presence of the particular cell or tissue mRNA in a sample using, e.g., *in situ* hybridization.

In other exemplary embodiments, the polynucleotides are used in diagnostics as expressed sequence tags for identifying expressed genes or, as well known in the art and exemplified by Vollrath et al., Science 258:52-59 (1992), as expressed sequence tags for physical mapping of the human genome.

The polypeptides according to the invention can be used in a variety of conventional procedures and methods that are currently applied to other proteins. For example, a polypeptide of the invention can be used to generate an antibody that specifically binds the polypeptide. Such antibodies, particularly monoclonal antibodies, are useful for detecting or quantitating the polypeptide in tissue. The polypeptides of the invention can also be used as molecular weight markers, and as a food supplement.

Methods are also provided for preventing, treating, or ameliorating a medical condition which comprises the step of administering to a mammalian subject a therapeutically effective amount of a composition comprising a polypeptide of the present invention and a pharmaceutically acceptable carrier.

In particular, the polypeptides and polynucleotides of the invention can be utilized, for example, in methods for the prevention and/or treatment of disorders involving aberrant protein expression or biological activity.

The present invention further relates to methods for detecting the presence of the  
5 polynucleotides or polypeptides of the invention in a sample. Such methods can, for example, be utilized as part of prognostic and diagnostic evaluation of disorders as recited herein and for the identification of subjects exhibiting a predisposition to such conditions. The invention provides a method for detecting the polynucleotides of the invention in a sample, comprising contacting the sample with a compound that binds to and forms a complex with the polynucleotide of  
10 interest for a period sufficient to form the complex and under conditions sufficient to form a complex and detecting the complex such that if a complex is detected, the polynucleotide of interest is detected. The invention also provides a method for detecting the polypeptides of the invention in a sample comprising contacting the sample with a compound that binds to and forms a complex with the polypeptide under conditions and for a period sufficient to form the complex  
15 and detecting the formation of the complex such that if a complex is formed, the polypeptide is detected.

The invention also provides kits comprising polynucleotide probes and/or monoclonal antibodies, and optionally quantitative standards, for carrying out methods of the invention. Furthermore, the invention provides methods for evaluating the efficacy of drugs, and  
20 monitoring the progress of patients, involved in clinical trials for the treatment of disorders as recited above.

The invention also provides methods for the identification of compounds that modulate (*i.e.*, increase or decrease) the expression or activity of the polynucleotides and/or polypeptides of the invention. Such methods can be utilized, for example, for the identification of compounds  
25 that can ameliorate symptoms of disorders as recited herein. Such methods can include, but are not limited to, assays for identifying compounds and other substances that interact with (*e.g.*, bind to) the polypeptides of the invention. The invention provides a method for identifying a compound that binds to the polypeptides of the invention comprising contacting the compound with a polypeptide of the invention in a cell for a time sufficient to form a  
30 polypeptide/compound complex, wherein the complex drives expression of a reporter gene sequence in the cell; and detecting the complex by detecting the reporter gene sequence expression such that if expression of the reporter gene is detected the compound that binds to a polypeptide of the invention is identified.

The methods of the invention also provides methods for treatment which involve the  
35 administration of the polynucleotides or polypeptides of the invention to individuals exhibiting

symptoms or tendencies. In addition, the invention encompasses methods for treating diseases or disorders as recited herein comprising administering compounds and other substances that modulate the overall activity of the target gene products. Compounds and other substances can effect such modulation either on the level of target gene/protein expression or target protein activity.

The polypeptides of the present invention and the polynucleotides encoding them are also useful for the same functions known to one of skill in the art as the polypeptides and polynucleotides to which they have homology (set forth in the sequence listing). If no homology is set forth for a sequence, then the polypeptides and polynucleotides of the present invention are useful for a variety of applications, as described herein, including use in arrays for detection.

## 4. DETAILED DESCRIPTION OF THE INVENTION

### 4.1 DEFINITIONS

It must be noted that as used herein and in the appended claims, the singular forms "a", "an" and "the" include plural references unless the context clearly dictates otherwise.

The term "active" refers to those forms of the polypeptide which retain the biologic and/or immunologic activities of any naturally occurring polypeptide. According to the invention, the terms "biologically active" or "biological activity" refer to a protein or peptide having structural, regulatory or biochemical functions of a naturally occurring molecule. Likewise "immunologically active" or "immunological activity" refers to the capability of the natural, recombinant or synthetic polypeptide to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "activated cells" as used in this application are those cells which are engaged in extracellular or intracellular membrane trafficking, including the export of secretory or enzymatic molecules as part of a normal or disease process.

The terms "complementary" or "complementarity" refer to the natural binding of polynucleotides by base pairing. For example, the sequence 5'-AGT-3' binds to the complementary sequence 3'-TCA-5'. Complementarity between two single-stranded molecules may be "partial" such that only some of the nucleic acids bind or it may be "complete" such that total complementarity exists between the single stranded molecules. The degree of complementarity between the nucleic acid strands has significant effects on the efficiency and strength of the hybridization between the nucleic acid strands.

The term "embryonic stem cells (ES)" refers to a cell that can give rise to many differentiated cell types in an embryo or an adult, including the germ cells. The term "germ line stem cells (GSCs)" refers to stem cells derived from primordial stem cells that provide a steady and continuous source of germ cells for the production of gametes. The term "primordial germ cells (PGCs)" refers to a small population of cells set aside from other cell lineages particularly from the yolk sac, mesenteries, or gonadal ridges during embryogenesis that have the potential to differentiate into germ cells and other cells. PGCs are the source from which GSCs and ES cells are derived. The PGCs, the GSCs and the ES cells are capable of self-renewal. Thus these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells that comprise the adult specialized organs, but are able to regenerate themselves.

The term "expression modulating fragment," EMF, means a series of nucleotides which modulates the expression of an operably linked ORF or another EMF.

As used herein, a sequence is said to "modulate the expression of an operably linked sequence" when the expression of the sequence is altered by the presence of the EMF. EMFs include, but are not limited to, promoters, and promoter modulating sequences (inducible elements). One class of EMFs are nucleic acid fragments which induce the expression of an operably linked ORF in response to a specific regulatory factor or physiological event.

The terms "nucleotide sequence" or "nucleic acid" or "polynucleotide" or "oligonucleotide" are used interchangeably and refer to a heteropolymer of nucleotides or the sequence of these nucleotides. These phrases also refer to DNA or RNA of genomic or synthetic origin which may be single-stranded or double-stranded and may represent the sense or the antisense strand, to peptide nucleic acid (PNA) or to any DNA-like or RNA-like material. In the sequences herein A is adenine, C is cytosine, T is thymine, G is guanine and N is A, C, G or T (U). It is contemplated that where the polynucleotide is RNA, the T (thymine) in the sequences provided herein is substituted with U (uracil). Generally, nucleic acid segments provided by this invention may be assembled from fragments of the genome and short oligonucleotide linkers, or from a series of oligonucleotides, or from individual nucleotides, to provide a synthetic nucleic acid which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon, or a eukaryotic gene.

The terms "oligonucleotide fragment" or a "polynucleotide fragment", "portion," or "segment" or "probe" or "primer" are used interchangeably and refer to a sequence of nucleotide residues which are at least about 5 nucleotides, more preferably at least about 7 nucleotides, more preferably at least about 9 nucleotides, more preferably at least about 11 nucleotides and most preferably at least about 17 nucleotides. The fragment is preferably less than about 500 nucleotides, preferably less than about 200 nucleotides, more preferably less than about 100

nucleotides, more preferably less than about 50 nucleotides and most preferably less than 30 nucleotides. Preferably the probe is from about 6 nucleotides to about 200 nucleotides, preferably from about 15 to about 50 nucleotides, more preferably from about 17 to 30 nucleotides and most preferably from about 20 to 25 nucleotides. Preferably the fragments can be used in polymerase chain reaction (PCR), various hybridization procedures or microarray procedures to identify or amplify identical or related parts of mRNA or DNA molecules. A fragment or segment may uniquely identify each polynucleotide sequence of the present invention. Preferably the fragment comprises a sequence substantially similar to any one of SEQ ID NO: 1-5497.

Probes may, for example, be used to determine whether specific mRNA molecules are present in a cell or tissue or to isolate similar nucleic acid sequences from chromosomal DNA as described by Walsh et al. (Walsh, P.S. et al., 1992, PCR Methods Appl 1:241-250). They may be labeled by nick translation, Klenow fill-in reaction, PCR, or other methods well known in the art. Probes of the present invention, their preparation and/or labeling are elaborated in Sambrook, J. et al., 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, NY; or Ausubel, F.M. et al., 1989, Current Protocols in Molecular Biology, John Wiley & Sons, New York NY, both of which are incorporated herein by reference in their entirety.

The nucleic acid sequences of the present invention also include the sequence information from the nucleic acid sequences of SEQ ID NO: 1-5497. The sequence information can be a segment of any one of SEQ ID NO: 1-5497 that uniquely identifies or represents the sequence information of that sequence of SEQ ID NO: 1-5497. One such segment can be a twenty-mer nucleic acid sequence because the probability that a twenty-mer is fully matched in the human genome is 1 in 300. In the human genome, there are three billion base pairs in one set of chromosomes. Because  $4^{20}$  possible twenty-mers exist, there are 300 times more twenty-mers than there are base pairs in a set of human chromosomes. Using the same analysis, the probability for a seventeen-mer to be fully matched in the human genome is approximately 1 in 5. When these segments are used in arrays for expression studies, fifteen-mer segments can be used. The probability that the fifteen-mer is fully matched in the expressed sequences is also approximately one in five because expressed sequences comprise less than approximately 5% of the entire genome sequence.

Similarly, when using sequence information for detecting a single mismatch, a segment can be a twenty-five mer. The probability that the twenty-five mer would appear in a human genome with a single mismatch is calculated by multiplying the probability for a full match ( $1/4^{25}$ ) times the increased probability for mismatch at each nucleotide position ( $3 \times 25$ ). The probability that an

eighteen mer with a single mismatch can be detected in an array for expression studies is approximately one in five. The probability that a twenty-mer with a single mismatch can be detected in a human genome is approximately one in five.

5 The term "open reading frame," ORF, means a series of nucleotide triplets coding for amino acids without any termination codons and is a sequence translatable into protein.

10 The terms "operably linked" or "operably associated" refer to functionally related nucleic acid sequences. For example, a promoter is operably associated or operably linked with a coding sequence if the promoter controls the transcription of the coding sequence. While operably linked nucleic acid sequences can be contiguous and in the same reading frame, certain genetic elements *e.g.* repressor genes are not contiguously linked to the coding sequence but still control transcription/translation of the coding sequence.

The term "pluripotent" refers to the capability of a cell to differentiate into a number of differentiated cell types that are present in an adult organism. A pluripotent cell is restricted in its differentiation capability in comparison to a totipotent cell.

15 The terms "polypeptide" or "peptide" or "amino acid sequence" refer to an oligopeptide, peptide, polypeptide or protein sequence or fragment thereof and to naturally occurring or synthetic molecules. A polypeptide "fragment," "portion," or "segment" is a stretch of amino acid residues of at least about 5 amino acids, preferably at least about 7 amino acids, more preferably at least about 9 amino acids and most preferably at least about 17 or more amino acids. The peptide preferably is not greater than about 200 amino acids, more preferably less than 150 amino acids and most preferably less than 100 amino acids. Preferably the peptide is from about 5 to about 200 amino acids. To be active, any polypeptide must have sufficient length to display biological and/or immunological activity.

25 The term "naturally occurring polypeptide" refers to polypeptides produced by cells that have not been genetically engineered and specifically contemplates various polypeptides arising from post-translational modifications of the polypeptide including, but not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and acylation.

The term "translated protein coding portion" means a sequence which encodes for the full length protein which may include any leader sequence or any processing sequence.

30 The term "mature protein coding sequence" means a sequence which encodes a peptide or protein without a signal or leader sequence. The "mature protein portion" means that portion of the protein which does not include a signal or leader sequence. The peptide may have been produced by processing in the cell which removes any leader/signal sequence. The mature protein portion may or may not include an initial methionine residue. The methionine residue may be removed from the protein during processing in the cell. The peptide may be produced

synthetically or the protein may have been produced using a polynucleotide only encoding for the mature protein coding sequence.

The term "derivative" refers to polypeptides chemically modified by such techniques as ubiquitination, labeling (*e.g.*, with radionuclides or various enzymes), covalent polymer  
5 attachment such as pegylation (derivatization with polyethylene glycol) and insertion or substitution by chemical synthesis of amino acids such as ornithine, which do not normally occur in human proteins.

The term "variant" (or "analog") refers to any polypeptide differing from naturally occurring polypeptides by amino acid insertions, deletions, and substitutions, created using, *e.g.*,  
10 recombinant DNA techniques. Guidance in determining which amino acid residues may be replaced, added or deleted without abolishing activities of interest, may be found by comparing the sequence of the particular polypeptide with that of homologous peptides and minimizing the number of amino acid sequence changes made in regions of high homology (conserved regions) or by replacing amino acids with consensus sequence.

Alternatively, recombinant variants encoding these same or similar polypeptides may be synthesized or selected by making use of the "redundancy" in the genetic code. Various codon  
15 substitutions, such as the silent changes which produce various restriction sites, may be introduced to optimize cloning into a plasmid or viral vector or expression in a particular prokaryotic or eukaryotic system. Mutations in the polynucleotide sequence may be reflected in the polypeptide or domains of other peptides added to the polypeptide to modify the properties of  
20 any part of the polypeptide, to change characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate.

Preferably, amino acid "substitutions" are the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, *i.e.*, conservative amino  
25 acid replacements. "Conservative" amino acid substitutions may be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity, and/or the amphipathic nature of the residues involved. For example, nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine; polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, asparagine, and  
30 glutamine; positively charged (basic) amino acids include arginine, lysine, and histidine; and negatively charged (acidic) amino acids include aspartic acid and glutamic acid. "Insertions" or "deletions" are preferably in the range of about 1 to 20 amino acids, more preferably 1 to 10 amino acids. The variation allowed may be experimentally determined by systematically making insertions, deletions, or substitutions of amino acids in a polypeptide molecule using  
35 recombinant DNA techniques and assaying the resulting recombinant variants for activity.



Alternatively, where alteration of function is desired, insertions, deletions or non-conservative alterations can be engineered to produce altered polypeptides. Such alterations can, for example, alter one or more of the biological functions or biochemical characteristics of the polypeptides of the invention. For example, such alterations may change polypeptide characteristics such as ligand-binding affinities, interchain affinities, or degradation/turnover rate. Further, such alterations can be selected so as to generate polypeptides that are better suited for expression, scale up and the like in the host cells chosen for expression. For example, cysteine residues can be deleted or substituted with another amino acid residue in order to eliminate disulfide bridges.

The terms "purified" or "substantially purified" as used herein denotes that the indicated nucleic acid or polypeptide is present in the substantial absence of other biological macromolecules, *e.g.*, polynucleotides, proteins, and the like. In one embodiment, the polynucleotide or polypeptide is purified such that it constitutes at least 95% by weight, more preferably at least 99% by weight, of the indicated biological macromolecules present (but water, buffers, and other small molecules, especially molecules having a molecular weight of less than 1000 daltons, can be present).

The term "isolated" as used herein refers to a nucleic acid or polypeptide separated from at least one other component (*e.g.*, nucleic acid or polypeptide) present with the nucleic acid or polypeptide in its natural source. In one embodiment, the nucleic acid or polypeptide is found in the presence of (if anything) only a solvent, buffer, ion, or other component normally present in a solution of the same. The terms "isolated" and "purified" do not encompass nucleic acids or polypeptides present in their natural source.

The term "recombinant," when used herein to refer to a polypeptide or protein, means that a polypeptide or protein is derived from recombinant (*e.g.*, microbial, insect, or mammalian) expression systems. "Microbial" refers to recombinant polypeptides or proteins made in bacterial or fungal (*e.g.*, yeast) expression systems. As a product, "recombinant microbial" defines a polypeptide or protein essentially free of native endogenous substances and unaccompanied by associated native glycosylation. Polypeptides or proteins expressed in most bacterial cultures, *e.g.*, *E. coli*, will be free of glycosylation modifications; polypeptides or proteins expressed in yeast will have a glycosylation pattern in general different from those expressed in mammalian cells.

The term "recombinant expression vehicle or vector" refers to a plasmid or phage or virus or vector, for expressing a polypeptide from a DNA (RNA) sequence. An expression vehicle can comprise a transcriptional unit comprising an assembly of (1) a genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers, (2) a structural

or coding sequence which is transcribed into mRNA and translated into protein, and (3) appropriate transcription initiation and termination sequences. Structural units intended for use in yeast or eukaryotic expression systems preferably include a leader sequence enabling extracellular secretion of translated protein by a host cell. Alternatively, where recombinant protein is expressed without a leader or transport sequence, it may include an amino terminal methionine residue. This residue may or may not be subsequently cleaved from the expressed recombinant protein to provide a final product.

The term "recombinant expression system" means host cells which have stably integrated a recombinant transcriptional unit into chromosomal DNA or carry the recombinant transcriptional unit extrachromosomally. Recombinant expression systems as defined herein will express heterologous polypeptides or proteins upon induction of the regulatory elements linked to the DNA segment or synthetic gene to be expressed. This term also means host cells which have stably integrated a recombinant genetic element or elements having a regulatory role in gene expression, for example, promoters or enhancers. Recombinant expression systems as defined herein will express polypeptides or proteins endogenous to the cell upon induction of the regulatory elements linked to the endogenous DNA segment or gene to be expressed. The cells can be prokaryotic or eukaryotic.

The term "secreted" includes a protein that is transported across or through a membrane, including transport as a result of signal sequences in its amino acid sequence when it is expressed in a suitable host cell. "Secreted" proteins include without limitation proteins secreted wholly (*e.g.*, soluble proteins) or partially (*e.g.*, receptors) from the cell in which they are expressed. "Secreted" proteins also include without limitation proteins that are transported across the membrane of the endoplasmic reticulum. "Secreted" proteins are also intended to include proteins containing non-typical signal sequences (*e.g.* Interleukin-1 Beta, see Krasney, P.A. and Young, P.R. (1992) Cytokine 4(2):134 -143) and factors released from damaged cells (*e.g.* Interleukin-1 Receptor Antagonist, see Arend, W.P. et. al. (1998) Annu. Rev. Immunol. 16:27-55)

Where desired, an expression vector may be designed to contain a "signal or leader sequence" which will direct the polypeptide through the membrane of a cell. Such a sequence may be naturally present on the polypeptides of the present invention or provided from heterologous protein sources by recombinant DNA techniques.

The term "stringent" is used to refer to conditions that are commonly understood in the art as stringent. Stringent conditions can include highly stringent conditions (*i.e.*, hybridization to filter-bound DNA in 0.5 M NaHPO<sub>4</sub>, 7% sodium dodecyl sulfate (SDS), 1 mM EDTA at 65°C, and washing in 0.1X SSC/0.1% SDS at 68°C), and moderately stringent conditions (*i.e.*,

washing in 0.2X SSC/0.1% SDS at 42°C). Other exemplary hybridization conditions are described herein in the examples.

In instances of hybridization of deoxyoligonucleotides, additional exemplary stringent hybridization conditions include washing in 6X SSC/0.05% sodium pyrophosphate at 37°C (for 14-base oligonucleotides), 48°C (for 17-base oligos), 55°C (for 20-base oligonucleotides), and 60°C (for 23-base oligonucleotides).

As used herein, "substantially equivalent" can refer both to nucleotide and amino acid sequences, for example a mutant sequence, that varies from a reference sequence by one or more substitutions, deletions, or additions, the net effect of which does not result in an adverse functional dissimilarity between the reference and subject sequences. Typically, such a substantially equivalent sequence varies from one of those listed herein by no more than about 35% (*i.e.*, the number of individual residue substitutions, additions, and/or deletions in a substantially equivalent sequence, as compared to the corresponding reference sequence, divided by the total number of residues in the substantially equivalent sequence is about 0.35 or less).

Such a sequence is said to have 65% sequence identity to the listed sequence. In one embodiment, a substantially equivalent, *e.g.*, mutant, sequence of the invention varies from a listed sequence by no more than 30% (70% sequence identity); in a variation of this embodiment, by no more than 25% (75% sequence identity); and in a further variation of this embodiment, by no more than 20% (80% sequence identity) and in a further variation of this embodiment, by no more than 10% (90% sequence identity) and in a further variation of this embodiment, by no more than 5% (95% sequence identity). Substantially equivalent, *e.g.*, mutant, amino acid sequences according to the invention preferably have at least 80% sequence identity with a listed amino acid sequence, more preferably at least 85% sequence identity, more preferably at least 90% sequence identity, more preferably at least 95% identity, more preferably at least 98% identity, and most preferably at least 99% identity. Substantially equivalent nucleotide sequences of the invention can have lower percent sequence identities, taking into account, for example, the redundancy or degeneracy of the genetic code. Preferably, nucleotide sequence has at least about 65% identity, more preferably at least about 75% identity, more preferably at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, and most preferably at least about 95% identity, more preferably at least about 98% sequence identity, and most preferably at least about 99% sequence identity. For the purposes of the present invention, sequences having substantially equivalent biological activity and substantially equivalent expression characteristics are considered substantially equivalent. For the purposes of determining equivalence, truncation of the mature sequence (*e.g.*, via a mutation which creates a spurious stop codon) should be

disregarded. Sequence identity may be determined, *e.g.*, using the Jotun Hein method (Hein, J. (1990) *Methods Enzymol.* 183:626-645). Identity between sequences can also be determined by other methods known in the art, *e.g.* by varying hybridization conditions.

The term "totipotent" refers to the capability of a cell to differentiate into all of the cell types of an adult organism.

The term "transformation" means introducing DNA into a suitable host cell so that the DNA is replicable, either as an extrachromosomal element, or by chromosomal integration. The term "transfection" refers to the taking up of an expression vector by a suitable host cell, whether or not any coding sequences are in fact expressed. The term "infection" refers to the introduction of nucleic acids into a suitable host cell by use of a virus or viral vector.

As used herein, an "uptake modulating fragment," UMF, means a series of nucleotides which mediate the uptake of a linked DNA fragment into a cell. UMFs can be readily identified using known UMFs as a target sequence or target motif with the computer-based systems described below. The presence and activity of a UMF can be confirmed by attaching the suspected UMF to a marker sequence. The resulting nucleic acid molecule is then incubated with an appropriate host under appropriate conditions and the uptake of the marker sequence is determined. As described above, a UMF will increase the frequency of uptake of a linked marker sequence.

Each of the above terms is meant to encompass all that is described for each, unless the context dictates otherwise.

## 4.2 NUCLEIC ACIDS OF THE INVENTION

Nucleotide sequences of the invention are set forth in the Sequence Listing.

The isolated polynucleotides of the invention include a polynucleotide comprising the nucleotide sequences of SEQ ID NO: 1-5497; a polynucleotide encoding any one of the peptide sequences of SEQ ID NO: 5498-10994; and a polynucleotide comprising the nucleotide sequence encoding the mature protein coding sequence of the polypeptides of any one of SEQ ID NO: 5498-10994. The polynucleotides of the present invention also include, but are not limited to, a polynucleotide that hybridizes under stringent conditions to (a) the complement of any of the nucleotides sequences of SEQ ID NO: 1-5497; (b) nucleotide sequences encoding any one of the amino acid sequences set forth in the Sequence Listing; (c) a polynucleotide which is an allelic variant of any polynucleotide recited above; (d) a polynucleotide which encodes a species homolog of any of the proteins recited above; or (e) a polynucleotide that encodes a polypeptide comprising a specific domain or truncation of the polypeptides of SEQ ID NO: 5498-10994. Domains of interest may depend on the nature of the encoded polypeptide; *e.g.*, domains in

receptor-like polypeptides include ligand-binding, extracellular, transmembrane, or cytoplasmic domains, or combinations thereof; domains in immunoglobulin-like proteins include the variable immunoglobulin-like domains; domains in enzyme-like polypeptides include catalytic and substrate binding domains; and domains in ligand polypeptides include receptor-binding domains.

The polynucleotides of the invention include naturally occurring or wholly or partially synthetic DNA, *e.g.*, cDNA and genomic DNA, and RNA, *e.g.*, mRNA. The polynucleotides may include all of the coding region of the cDNA or may represent a portion of the coding region of the cDNA.

The present invention also provides genes corresponding to the cDNA sequences disclosed herein. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. Further 5' and 3' sequence can be obtained using methods known in the art. For example, full length cDNA or genomic DNA that corresponds to any of the polynucleotides of SEQ ID NO: 1-5497 can be obtained by screening appropriate cDNA or genomic DNA libraries under suitable hybridization conditions using any of the polynucleotides of SEQ ID NO: 1-5497 or a portion thereof as a probe. Alternatively, the polynucleotides of SEQ ID NO: 1-5497 may be used as the basis for suitable primer(s) that allow identification and/or amplification of genes in appropriate genomic DNA or cDNA libraries.

The nucleic acid sequences of the invention can be assembled from ESTs and sequences (including cDNA and genomic sequences) obtained from one or more public databases, such as dbEST, gbpr, and UniGene. The EST sequences can provide identifying sequence information, representative fragment or segment information, or novel segment information for the full-length gene.

The polynucleotides of the invention also provide polynucleotides including nucleotide sequences that are substantially equivalent to the polynucleotides recited above. Polynucleotides according to the invention can have, *e.g.*, at least about 65%, at least about 70%, at least about 75%, at least about 80%, 81%, 82%, 83%, 84%, more typically at least about 85%, 86%, 87%, 88%, 89%, more typically at least about 90%, 91%, 92%, 93%, 94%, and even more typically at least about 95%, 96%, 97%, 98%, 99%, sequence identity to a polynucleotide recited above.

Included within the scope of the nucleic acid sequences of the invention are nucleic acid sequence fragments that hybridize under stringent conditions to any of the nucleotide sequences of SEQ ID NO: 1-5497, or complements thereof, which fragment is greater than about 5 nucleotides, preferably 7 nucleotides, more preferably greater than 9 nucleotides and most

preferably greater than 17 nucleotides. Fragments of, *e.g.* 15, 17, or 20 nucleotides or more that are selective for (*i.e.* specifically hybridize to any one of the polynucleotides of the invention) are contemplated. Probes capable of specifically hybridizing to a polynucleotide can differentiate polynucleotide sequences of the invention from other polynucleotide sequences in the same family of genes or can differentiate human genes from genes of other species, and are preferably based on unique nucleotide sequences.

The sequences falling within the scope of the present invention are not limited to these specific sequences, but also include allelic and species variations thereof. Allelic and species variations can be routinely determined by comparing the sequence provided in SEQ ID NO: 1-5497, a representative fragment thereof, or a nucleotide sequence at least 90% identical, preferably 95% identical, to SEQ ID NO: 1-5497 with a sequence from another isolate of the same species. Furthermore, to accommodate codon variability, the invention includes nucleic acid molecules coding for the same amino acid sequences as do the specific ORFs disclosed herein. In other words, in the coding region of an ORF, substitution of one codon for another codon that encodes the same amino acid is expressly contemplated.

The nearest neighbor or homology result for the nucleic acids of the present invention, including SEQ ID NO: 1-5497 can be obtained by searching a database using an algorithm or a program. Preferably, a BLAST which stands for Basic Local Alignment Search Tool is used to search for local sequence alignments (Altschul, S.F. J Mol. Evol. 36 290-300 (1993) and Altschul S.F. et al. J. Mol. Biol. 21:403-410 (1990)). Alternatively a FASTA version 3 search against Genpept, using Fastxy algorithm.

Species homologs (or orthologs) of the disclosed polynucleotides and proteins are also provided by the present invention. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous or related to that encoded by the polynucleotides.

The nucleic acid sequences of the invention are further directed to sequences which encode variants of the described nucleic acids. These amino acid sequence variants may be prepared by methods known in the art by introducing appropriate nucleotide changes into a native or variant polynucleotide. There are two variables in the construction of amino acid sequence variants: the location of the mutation and the nature of the mutation. Nucleic acids encoding the amino acid sequence variants are preferably constructed by mutating the

polynucleotide to encode an amino acid sequence that does not occur in nature. These nucleic acid alterations can be made at sites that differ in the nucleic acids from different species (variable positions) or in highly conserved regions (constant regions). Sites at such locations will typically be modified in series, *e.g.*, by substituting first with conservative choices (*e.g.*, hydrophobic amino acid to a different hydrophobic amino acid) and then with more distant choices (*e.g.*, hydrophobic amino acid to a charged amino acid), and then deletions or insertions may be made at the target site. Amino acid sequence deletions generally range from about 1 to 30 residues, preferably about 1 to 10 residues, and are typically contiguous. Amino acid insertions include amino- and/or carboxyl-terminal fusions ranging in length from one to one hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Intrasequence insertions may range generally from about 1 to 10 amino residues, preferably from 1 to 5 residues. Examples of terminal insertions include the heterologous signal sequences necessary for secretion or for intracellular targeting in different host cells and sequences such as FLAG or poly-histidine sequences useful for purifying the expressed protein.

In a preferred method, polynucleotides encoding the novel amino acid sequences are changed via site-directed mutagenesis. This method uses oligonucleotide sequences to alter a polynucleotide to encode the desired amino acid variant, as well as sufficient adjacent nucleotides on both sides of the changed amino acid to form a stable duplex on either side of the site of being changed. In general, the techniques of site-directed mutagenesis are well known to those of skill in the art and this technique is exemplified by publications such as, Edelman et al., *DNA* 2:183 (1983). A versatile and efficient method for producing site-specific changes in a polynucleotide sequence was published by Zoller and Smith, *Nucleic Acids Res.* 10:6487-6500 (1982). PCR may also be used to create amino acid sequence variants of the novel nucleic acids. When small amounts of template DNA are used as starting material, primer(s) that differs slightly in sequence from the corresponding region in the template DNA can generate the desired amino acid variant. PCR amplification results in a population of product DNA fragments that differ from the polynucleotide template encoding the polypeptide at the position specified by the primer. The product DNA fragments replace the corresponding region in the plasmid and this gives a polynucleotide encoding the desired amino acid variant.

A further technique for generating amino acid variants is the cassette mutagenesis technique described in Wells et al., *Gene* 34:315 (1985); and other mutagenesis techniques well known in the art, such as, for example, the techniques in Sambrook et al., *supra*, and *Current Protocols in Molecular Biology*, Ausubel et al. Due to the inherent degeneracy of the genetic code, other DNA sequences which encode substantially the same or a functionally equivalent amino acid sequence may be used in the practice of the invention for the cloning and expression

of these novel nucleic acids. Such DNA sequences include those which are capable of hybridizing to the appropriate novel nucleic acid sequence under stringent conditions.

Polynucleotides encoding preferred polypeptide truncations of the invention can be used to generate polynucleotides encoding chimeric or fusion proteins comprising one or more domains of the invention and heterologous protein sequences.

The polynucleotides of the invention additionally include the complement of any of the polynucleotides recited above. The polynucleotide can be DNA (genomic, cDNA, amplified, or synthetic) or RNA. Methods and algorithms for obtaining such polynucleotides are well known to those of skill in the art and can include, for example, methods for determining hybridization conditions that can routinely isolate polynucleotides of the desired sequence identities.

In accordance with the invention, polynucleotide sequences comprising the mature protein coding sequences corresponding to any one of SEQ ID NO: 1-5497, or functional equivalents thereof, may be used to generate recombinant DNA molecules that direct the expression of that nucleic acid, or a functional equivalent thereof, in appropriate host cells. Also included are the cDNA inserts of any of the clones identified herein.

A polynucleotide according to the invention can be joined to any of a variety of other nucleotide sequences by well-established recombinant DNA techniques (see Sambrook J et al. (1989) *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratory, NY). Useful nucleotide sequences for joining to polynucleotides include an assortment of vectors, *e.g.*, plasmids, cosmids, lambda phage derivatives, phagemids, and the like, that are well known in the art. Accordingly, the invention also provides a vector including a polynucleotide of the invention and a host cell containing the polynucleotide. In general, the vector contains an origin of replication functional in at least one organism, convenient restriction endonuclease sites, and a selectable marker for the host cell. Vectors according to the invention include expression vectors, replication vectors, probe generation vectors, and sequencing vectors. A host cell according to the invention can be a prokaryotic or eukaryotic cell and can be a unicellular organism or part of a multicellular organism.

The present invention further provides recombinant constructs comprising a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-5497 or a fragment thereof or any other polynucleotides of the invention. In one embodiment, the recombinant constructs of the present invention comprise a vector, such as a plasmid or viral vector, into which a nucleic acid having any of the nucleotide sequences of SEQ ID NO: 1-5497 or a fragment thereof is inserted, in a forward or reverse orientation. In the case of a vector comprising one of the ORFs of the present invention, the vector may further comprise regulatory sequences, including for example, a promoter, operably linked to the ORF. Large numbers of suitable vectors and promoters are



known to those of skill in the art and are commercially available for generating the recombinant constructs of the present invention. The following vectors are provided by way of example.

Bacterial: pBs, phagescript, PsiX174, pBluescript SK, pBs KS, pNH8a, pNH16a, pNH18a, pNH46a (Stratagene); pTrc99A, pKK223-3, pDR540, pRIT5 (Pharmacia).

- 5 Eukaryotic: pWLneo, pSV2cat, pOG44, PXTI, pSG (Stratagene) pSVK3, pBPV, pMSG, pSVL (Pharmacia).

The isolated polynucleotide of the invention may be operably linked to an expression control sequence such as the pMT2 or pED expression vectors disclosed in Kaufman et al., *Nucleic Acids Res.* 19, 4485-4490 (1991), in order to produce the protein recombinantly. Many  
10 suitable expression control sequences are known in the art. General methods of expressing recombinant proteins are also known and are exemplified in R. Kaufman, *Methods in Enzymology* 185, 537-566 (1990). As defined herein "operably linked" means that the isolated polynucleotide of the invention and an expression control sequence are situated within a vector or cell in such a way that the protein is expressed by a host cell which has been transformed  
15 (transfected) with the ligated polynucleotide/expression control sequence.

Promoter regions can be selected from any desired gene using CAT (chloramphenicol transferase) vectors or other vectors with selectable markers. Two appropriate vectors are pKK232-8 and pCM7. Particular named bacterial promoters include lacI, lacZ, T3, T7, gpt, lambda PR, and trc. Eukaryotic promoters include CMV immediate early, HSV thymidine  
20 kinase, early and late SV40, LTRs from retrovirus, and mouse metallothionein-I. Selection of the appropriate vector and promoter is well within the level of ordinary skill in the art. Generally, recombinant expression vectors will include origins of replication and selectable markers permitting transformation of the host cell, e.g., the ampicillin resistance gene of *E. coli* and *S. cerevisiae* TRP1 gene, and a promoter derived from a highly-expressed gene to direct  
25 transcription of a downstream structural sequence. Such promoters can be derived from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), a-factor, acid phosphatase, or heat shock proteins, among others. The heterologous structural sequence is assembled in appropriate phase with translation initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein into the  
30 periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an amino terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product. Useful expression vectors for bacterial use are constructed by inserting a structural DNA sequence encoding a desired protein together with suitable translation initiation and termination  
35 signals in operable reading phase with a functional promoter. The vector will comprise one or

more phenotypic selectable markers and an origin of replication to ensure maintenance of the vector and to, if desirable, provide amplification within the host. Suitable prokaryotic hosts for transformation include *E. coli*, *Bacillus subtilis*, *Salmonella typhimurium* and various species within the genera *Pseudomonas*, *Streptomyces*, and *Staphylococcus*, although others may also be employed as a matter of choice.

As a representative but non-limiting example, useful expression vectors for bacterial use can comprise a selectable marker and bacterial origin of replication derived from commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017). Such commercial vectors include, for example, pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden) and GEM 1 (Promega Biotech, Madison, WI, USA). These pBR322 "backbone" sections are combined with an appropriate promoter and the structural sequence to be expressed. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter is induced or derepressed by appropriate means (*e.g.*, temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification.

Polynucleotides of the invention can also be used to induce immune responses. For example, as described in Fan et al., *Nat. Biotech.* 17:870-872 (1999), incorporated herein by reference, nucleic acid sequences encoding a polypeptide may be used to generate antibodies against the encoded polypeptide following topical administration of naked plasmid DNA or following injection, and preferably intramuscular injection of the DNA. The nucleic acid sequences are preferably inserted in a recombinant expression vector and may be in the form of naked DNA.

#### 4.3 ANTISENSE

Another aspect of the invention pertains to isolated antisense nucleic acid molecules that are hybridizable to or complementary to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1-5497, or fragments, analogs or derivatives thereof. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. In specific aspects, antisense nucleic acid molecules are provided that comprise a sequence complementary to at least about 10, 25, 50, 100, 250 or 500 nucleotides or an entire coding strand, or to only a portion thereof. Nucleic acid molecules encoding fragments, homologs, derivatives and analogs of a protein of any of SEQ ID

NO: 5498-10994 or antisense nucleic acids complementary to a nucleic acid sequence of SEQ ID NO: 1-5497 are additionally provided.

In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence of the invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues. In another embodiment, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequences encoding a nucleic acid disclosed herein (*e.g.*, SEQ ID NO: 1-5497), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick or Hoogsteen base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of a mRNA, but more preferably is an oligonucleotide that is antisense to only a portion of the coding or noncoding region of a mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of a mRNA. An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis or enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives and acridine substituted nucleotides can be used.

Examples of modified nucleotides that can be used to generate the antisense nucleic acid include: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the

antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

5           The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a protein according to the invention to thereby inhibit expression of the protein, *e.g.*, by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of  
10 an antisense nucleic acid molecule that binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified  
15 such that they specifically bind to receptors or antigens expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecules to peptides or antibodies that bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the  
20 control of a strong pol II or pol III promoter are preferred.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gaultier *et al.* (1987) *Nucleic Acids Res* 15: 6625-6641). The  
25 antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.* (1987) *Nucleic Acids Res* 15: 6131-6148) or a chimeric RNA-DNA analogue (Inoue *et al.* (1987) *FEBS Lett* 215: 327-330).

#### 4.4 RIBOZYMES AND PNA MOIETIES

30           In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as a mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave a mRNA transcripts to thereby inhibit  
35 translation of a mRNA. A ribozyme having specificity for a nucleic acid of the invention can be

designed based upon the nucleotide sequence of a DNA disclosed herein (*i.e.*, SEQ ID NO: 1-5497). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an mRNA of SEQ ID NO: 1-5497 (see, *e.g.*, Cech *et al.* U.S. Pat. No. 4,987,071; and Cech *et al.* U.S. Pat. No. 5,116,742). Alternatively, polynucleotides of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel *et al.*, (1993) *Science* 261:1411-1418.

Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region (*e.g.*, promoter and/or enhancers) to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene. (1991) *Anticancer Drug Des.* 6: 569-84; Helene. *et al.* (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14: 807-15.

In various embodiments, the nucleic acids of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, *e.g.*, the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate peptide nucleic acids (see Hyrup *et al.* (1996) *Bioorg Med Chem* 4: 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, *e.g.*, DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup *et al.* (1996) above; Perry-O'Keefe *et al.* (1996) *PNAS* 93: 14670-675.

PNAs of the invention can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, *e.g.*, inducing transcription or translation arrest or inhibiting replication. PNAs of the invention can also be used, *e.g.*, in the analysis of single base pair mutations in a gene by, *e.g.*, PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, *e.g.*, S1 nucleases (Hyrup B. (1996) above); or as probes or primers for DNA sequence and hybridization (Hyrup *et al.* (1996), above; Perry-O'Keefe (1996), above).

In another embodiment, PNAs of the invention can be modified, *e.g.*, to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras can be generated that may

combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, *e.g.*, RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) above). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) above and Finn *et al.* (1996) *Nucl Acids Res* 24: 3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry, and modified nucleoside analogs, *e.g.*, 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite, can be used between the PNA and the 5' end of DNA (Mag *et al.* (1989) *Nucl Acid Res* 17: 5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn *et al.* (1996) above). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment. See, Petersen *et al.* (1975) *Bioorg Med Chem Lett* 5: 1119-11124.

In other embodiments, the oligonucleotide may include other appended groups such as peptides (*e.g.*, for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, *e.g.*, Letsinger *et al.*, 1989, *Proc. Natl. Acad. Sci. U.S.A.* 86:6553-6556; Lemaitre *et al.*, 1987, *Proc. Natl. Acad. Sci.* 84:648-652; PCT Publication No. W088/09810) or the blood-brain barrier (see, *e.g.*, PCT Publication No. W089/10134). In addition, oligonucleotides can be modified with hybridization triggered cleavage agents (See, *e.g.*, Krol *et al.*, 1988, *BioTechniques* 6:958-976) or intercalating agents (see, *e.g.*, Zon, 1988, *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, *e.g.*, a peptide, a hybridization triggered cross-linking agent, a transport agent, a hybridization-triggered cleavage agent, etc.

#### 4.5 HOSTS

The present invention further provides host cells genetically engineered to contain the polynucleotides of the invention. For example, such host cells may contain nucleic acids of the invention introduced into the host cell using known transformation, transfection or infection methods. The present invention still further provides host cells genetically engineered to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in the cell.

Knowledge of nucleic acid sequences allows for modification of cells to permit, or increase, expression of endogenous polypeptide. Cells can be modified (*e.g.*, by homologous

recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the polypeptide at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the encoding sequences. See, for example, PCT International Publication No. WO94/12650, PCT International Publication No. WO92/20808, and PCT International Publication No. WO91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, *ada*, *dhfr*, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the coding sequence, amplification of the marker DNA by standard selection methods results in co-amplification of the desired protein coding sequences in the cells.

The host cell can be a higher eukaryotic host cell, such as a mammalian cell, a lower eukaryotic host cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. Introduction of the recombinant construct into the host cell can be effected by calcium phosphate transfection, DEAE, dextran mediated transfection, or electroporation (Davis, L. et al., *Basic Methods in Molecular Biology* (1986)). The host cells containing one of the polynucleotides of the invention, can be used in conventional manners to produce the gene product encoded by the isolated fragment (in the case of an ORF) or can be used to produce a heterologous protein under the control of the EMF.

Any host/vector system can be used to express one or more of the ORFs of the present invention. These include, but are not limited to, eukaryotic hosts such as HeLa cells, Cv-1 cell, COS cells, 293 cells, and Sf9 cells, as well as prokaryotic host such as *E. coli* and *B. subtilis*. The most preferred cells are those which do not normally express the particular polypeptide or protein or which expresses the polypeptide or protein at low natural level. Mature proteins can be expressed in mammalian cells, yeast, bacteria, or other cells under the control of appropriate promoters. Cell-free translation systems can also be employed to produce such proteins using RNAs derived from the DNA constructs of the present invention. Appropriate cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., in *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor, New York (1989), the disclosure of which is hereby incorporated by reference.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts, described by Gluzman, *Cell* 23:175 (1981). Other cell lines capable of expressing a compatible vector are, for example, the C127, monkey COS cells, Chinese Hamster Ovary (CHO) cells, human kidney 293 cells, human epidermal A431 cells, human Colo205 cells, 3T3

cells, CV-1 cells, other transformed primate cell lines, normal diploid cells, cell strains derived from *in vitro* culture of primary tissue, primary explants, HeLa cells, mouse L cells, BHK, HL-60, U937, HaK or Jurkat cells. Mammalian expression vectors will comprise an origin of replication, a suitable promoter and also any necessary ribosome binding sites, polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. DNA sequences derived from the SV40 viral genome, for example, SV40 origin, early promoter, enhancer, splice, and polyadenylation sites may be used to provide the required nontranscribed genetic elements. Recombinant polypeptides and proteins produced in bacterial culture are usually isolated by initial extraction from cell pellets, followed by one or more salting-out, aqueous ion exchange or size exclusion chromatography steps. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high performance liquid chromatography (HPLC) can be employed for final purification steps. Microbial cells employed in expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents.

Alternatively, it may be possible to produce the protein in lower eukaryotes such as yeast or insects or in prokaryotes such as bacteria. Potentially suitable yeast strains include *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, *Kluyveromyces* strains, *Candida*, or any yeast strain capable of expressing heterologous proteins. Potentially suitable bacterial strains include *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhimurium*, or any bacterial strain capable of expressing heterologous proteins. If the protein is made in yeast or bacteria, it may be necessary to modify the protein produced therein, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain the functional protein. Such covalent attachments may be accomplished using known chemical or enzymatic methods.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequence include polyadenylation signals, mRNA stability elements, splice



sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally occurring elements. Here, the naturally occurring sequences are deleted and new sequences are added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the host cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (*gpt*) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

#### 4.6 POLYPEPTIDES OF THE INVENTION

The isolated polypeptides of the invention include, but are not limited to, a polypeptide comprising: the amino acid sequences set forth as any one of SEQ ID NO: 5498-10994 or an amino acid sequence encoded by any one of the nucleotide sequences SEQ ID NO: 1-5497 or the corresponding full length or mature protein. Polypeptides of the invention also include polypeptides preferably with biological or immunological activity that are encoded by: (a) a polynucleotide having any one of the nucleotide sequences set forth in SEQ ID NO: 1-5497 or

(b) polynucleotides encoding any one of the amino acid sequences set forth as SEQ ID NO: 5498-10994 or (c) polynucleotides that hybridize to the complement of the polynucleotides of either (a) or (b) under stringent hybridization conditions. The invention also provides biologically active or immunologically active variants of any of the amino acid sequences set forth as SEQ ID NO: 5498-10994 or the corresponding full length or mature protein; and "substantial equivalents" thereof (*e.g.*, with at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, 86%, 87%, 88%, 89%, at least about 90%, 91%, 92%, 93%, 94%, typically at least about 95%, 96%, 97%, more typically at least about 98%, or most typically at least about 99% amino acid identity) that retain biological activity.

Polypeptides encoded by allelic variants may have a similar, increased, or decreased activity compared to polypeptides comprising SEQ ID NO: 5498-10994.

Fragments of the proteins of the present invention which are capable of exhibiting biological activity are also encompassed by the present invention. Fragments of the protein may be in linear form or they may be cyclized using known methods, for example, as described in H. U. Saragovi, et al., *Bio/Technology* 10, 773-778 (1992) and in R. S. McDowell, et al., *J. Amer. Chem. Soc.* 114, 9245-9253 (1992), both of which are incorporated herein by reference. Such fragments may be fused to carrier molecules such as immunoglobulins for many purposes, including increasing the valency of protein binding sites.

The present invention also provides both full-length and mature forms (for example, without a signal sequence or precursor sequence) of the disclosed proteins. The protein coding sequence is identified in the sequence listing by translation of the disclosed nucleotide sequences. The mature form of such protein may be obtained by expression of a full-length polynucleotide in a suitable mammalian cell or other host cell. The sequence of the mature form of the protein is also determinable from the amino acid sequence of the full-length form. Where proteins of the present invention are membrane bound, soluble forms of the proteins are also provided. In such forms, part or all of the regions causing the proteins to be membrane bound are deleted so that the proteins are fully secreted from the cell in which they are expressed.

Protein compositions of the present invention may further comprise an acceptable carrier, such as a hydrophilic, *e.g.*, pharmaceutically acceptable, carrier.

The present invention further provides isolated polypeptides encoded by the nucleic acid fragments of the present invention or by degenerate variants of the nucleic acid fragments of the present invention. By "degenerate variant" is intended nucleotide fragments which differ from a nucleic acid fragment of the present invention (*e.g.*, an ORF) by nucleotide sequence but, due to the degeneracy of the genetic code, encode an identical polypeptide sequence. Preferred nucleic acid fragments of the present invention are the ORFs that encode proteins.

A variety of methodologies known in the art can be utilized to obtain any one of the isolated polypeptides or proteins of the present invention. At the simplest level, the amino acid sequence can be synthesized using commercially available peptide synthesizers. The synthetically-constructed protein sequences, by virtue of sharing primary, secondary or tertiary structural and/or conformational characteristics with proteins may possess biological properties in common therewith, including protein activity. This technique is particularly useful in producing small peptides and fragments of larger polypeptides. Fragments are useful, for example, in generating antibodies against the native polypeptide. Thus, they may be employed as biologically active or immunological substitutes for natural, purified proteins in screening of therapeutic compounds and in immunological processes for the development of antibodies.

The polypeptides and proteins of the present invention can alternatively be purified from cells which have been altered to express the desired polypeptide or protein. As used herein, a cell is said to be altered to express a desired polypeptide or protein when the cell, through genetic manipulation, is made to produce a polypeptide or protein which it normally does not produce or which the cell normally produces at a lower level. One skilled in the art can readily adapt procedures for introducing and expressing either recombinant or synthetic sequences into eukaryotic or prokaryotic cells in order to generate a cell which produces one of the polypeptides or proteins of the present invention.

The invention also relates to methods for producing a polypeptide comprising growing a culture of host cells of the invention in a suitable culture medium, and purifying the protein from the cells or the culture in which the cells are grown. For example, the methods of the invention include a process for producing a polypeptide in which a host cell containing a suitable expression vector that includes a polynucleotide of the invention is cultured under conditions that allow expression of the encoded polypeptide. The polypeptide can be recovered from the culture, conveniently from the culture medium, or from a lysate prepared from the host cells and further purified. Preferred embodiments include those in which the protein produced by such process is a full length or mature form of the protein.

In an alternative method, the polypeptide or protein is purified from bacterial cells which naturally produce the polypeptide or protein. One skilled in the art can readily follow known methods for isolating polypeptides and proteins in order to obtain one of the isolated polypeptides or proteins of the present invention. These include, but are not limited to, immunochromatography, HPLC, size-exclusion chromatography, ion-exchange chromatography, and immuno-affinity chromatography. See, *e.g.*, Scopes, *Protein Purification: Principles and Practice*, Springer-Verlag (1994); Sambrook, et al., in *Molecular Cloning: A Laboratory Manual*; Ausubel et al., *Current Protocols in Molecular Biology*. Polypeptide fragments that

retain biological/immunological activity include fragments comprising greater than about 100 amino acids, or greater than about 200 amino acids, and fragments that encode specific protein domains.

The purified polypeptides can be used in *in vitro* binding assays which are well known in the art to identify molecules which bind to the polypeptides. These molecules include but are not limited to, for *e.g.*, small molecules, molecules from combinatorial libraries, antibodies or other proteins. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

In addition, the peptides of the invention or molecules capable of binding to the peptides may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for SEQ ID NO: 5498-10994.

The protein of the invention may also be expressed as a product of transgenic animals, *e.g.*, as a component of the milk of transgenic cows, goats, pigs, or sheep which are characterized by somatic or germ cells containing a nucleotide sequence encoding the protein.

The proteins provided herein also include proteins characterized by amino acid sequences similar to those of purified proteins but into which modification are naturally provided or deliberately engineered. For example, modifications in the peptide or DNA sequence can be made by those skilled in the art using known techniques. Modifications of interest in the protein sequences may include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue in the coding sequence. For example, one or more of the cysteine residues may be deleted or replaced with another amino acid to alter the conformation of the molecule. Techniques for such alteration, substitution, replacement, insertion or deletion are well known to those skilled in the art (see, *e.g.*, U.S. Pat. No. 4,518,584). Preferably, such alteration, substitution, replacement, insertion or deletion retains the desired activity of the protein. Regions of the protein that are important for the protein function can be determined by various methods known in the art including the alanine-scanning method which involved systematic substitution of single or strings of amino acids with alanine, followed by testing the resulting alanine-containing variant for biological activity. This type of analysis determines the importance of the substituted amino acid(s) in biological activity. Regions of the protein that are important for protein function may be determined by the eMATRIX program.

Other fragments and derivatives of the sequences of proteins which would be expected to retain protein activity in whole or in part and are useful for screening or other immunological

methodologies may also be easily made by those skilled in the art given the disclosures herein. Such modifications are encompassed by the present invention.

The protein may also be produced by operably linking the isolated polynucleotide of the invention to suitable control sequences in one or more insect expression vectors, and employing an insect expression system. Materials and methods for baculovirus/insect cell expression systems are commercially available in kit form from, *e.g.*, Invitrogen, San Diego, Calif., U.S.A. (the MaxBat™ kit), and such methods are well known in the art, as described in Summers and Smith, Texas Agricultural Experiment Station Bulletin No. 1555 (1987), incorporated herein by reference. As used herein, an insect cell capable of expressing a polynucleotide of the present invention is "transformed."

The protein of the invention may be prepared by culturing transformed host cells under culture conditions suitable to express the recombinant protein. The resulting expressed protein may then be purified from such culture (*i.e.*, from culture medium or cell extracts) using known purification processes, such as gel filtration and ion exchange chromatography. The purification of the protein may also include an affinity column containing agents which will bind to the protein; one or more column steps over such affinity resins as concanavalin A-agarose, heparin-toyopearl™ or Cibacrom blue 3GA Sepharose™; one or more steps involving hydrophobic interaction chromatography using such resins as phenyl ether, butyl ether, or propyl ether; or immunoaffinity chromatography.

Alternatively, the protein of the invention may also be expressed in a form that will facilitate purification. For example, it may be expressed as a fusion protein, such as those of maltose binding protein (MBP), glutathione-S-transferase (GST) or thioredoxin (TRX), or as a His-tag. Kits for expression and purification of such fusion proteins are commercially available from New England BioLab (Beverly, Mass.), Pharmacia (Piscataway, N.J.) and Invitrogen, respectively. The protein can also be tagged with an epitope and subsequently purified by using a specific antibody directed to such epitope. One such epitope ("FLAG®") is commercially available from Kodak (New Haven, Conn.).

Finally, one or more reverse-phase high performance liquid chromatography (RP- HPLC) steps employing hydrophobic RP-HPLC media, *e.g.*, silica gel having pendant methyl or other aliphatic groups, can be employed to further purify the protein. Some or all of the foregoing purification steps, in various combinations, can also be employed to provide a substantially homogeneous isolated recombinant protein. The protein thus purified is substantially free of other mammalian proteins and is defined in accordance with the present invention as an "isolated protein."

The polypeptides of the invention include analogs (variants). This embraces fragments, as well as peptides in which one or more amino acids has been deleted, inserted, or substituted. Also, analogs of the polypeptides of the invention embrace fusions of the polypeptides or modifications of the polypeptides of the invention, wherein the polypeptide or analog is fused to another moiety or moieties, *e.g.*, targeting moiety or another therapeutic agent. Such analogs may exhibit improved properties such as activity and/or stability. Examples of moieties which may be fused to the polypeptide or an analog include, for example, targeting moieties which provide for the delivery of polypeptide to pancreatic cells, *e.g.*, antibodies to pancreatic cells, antibodies to immune cells such as T-cells, monocytes, dendritic cells, granulocytes, etc., as well as receptor and ligands expressed on pancreatic or immune cells. Other moieties which may be fused to the polypeptide include therapeutic agents which are used for treatment, for example, immunosuppressive drugs such as cyclosporin, SK506, azathioprine, CD3 antibodies and steroids. Also, polypeptides may be fused to immune modulators, and other cytokines such as alpha or beta interferon.

#### 4.6.1 DETERMINING POLYPEPTIDE AND POLYNUCLEOTIDE IDENTITY AND SIMILARITY

Preferred identity and/or similarity are designed to give the largest match between the sequences tested. Methods to determine identity and similarity are codified in computer programs including, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12(1):387 (1984); Genetics Computer Group, University of Wisconsin, Madison, WI), BLASTP, BLASTN, BLASTX, FASTA (Altschul, S.F. et al., J. Molec. Biol. 215:403-410 (1990), PSI-BLAST (Altschul S.F. et al., Nucleic Acids Res. vol. 25, pp. 3389-3402, herein incorporated by reference), eMatrix software (Wu et al., J. Comp. Biol., Vol. 6, pp. 219-235 (1999), herein incorporated by reference), eMotif software (Nevill-Manning et al, ISMB-97, Vol. 4, pp. 202-209, herein incorporated by reference), pFam software (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1), pp. 320-322 (1998), herein incorporated by reference) and the Kyte-Doolittle hydrophobicity prediction algorithm (J. Mol Biol, 157, pp. 105-31 (1982), incorporated herein by reference). The BLAST programs are publicly available from the National Center for Biotechnology Information (NCBI) and other sources (BLAST Manual, Altschul, S., et al. NCB NLM NIH Bethesda, MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990).

#### 4.7 CHIMERIC AND FUSION PROTEINS

The invention also provides chimeric or fusion proteins. As used herein, a "chimeric protein" or "fusion protein" comprises a polypeptide of the invention operatively linked to

another polypeptide. Within a fusion protein the polypeptide according to the invention can correspond to all or a portion of a protein according to the invention. In one embodiment, a fusion protein comprises at least one biologically active portion of a protein according to the invention. In another embodiment, a fusion protein comprises at least two biologically active portions of a protein according to the invention. Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide according to the invention and the other polypeptide are fused in-frame to each other. The polypeptide can be fused to the N-terminus or C-terminus.

For example, in one embodiment a fusion protein comprises a polypeptide according to the invention operably linked to the extracellular domain of a second protein.

In another embodiment, the fusion protein is a GST-fusion protein in which the polypeptide sequences of the invention are fused to the C-terminus of the GST (*i.e.*, glutathione S-transferase) sequences.

In another embodiment, the fusion protein is an immunoglobulin fusion protein in which the polypeptide sequences according to the invention comprises one or more domains are fused to sequences derived from a member of the immunoglobulin protein family. The immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a ligand and a protein of the invention on the surface of a cell, to thereby suppress signal transduction *in vivo*.

The immunoglobulin fusion proteins can be used to affect the bioavailability of a cognate ligand. Inhibition of the ligand/protein interaction may be useful therapeutically for both the treatment of proliferative and differentiative disorders, *e.g.*, cancer as well as modulating (*e.g.*, promoting or inhibiting) cell survival. Moreover, the immunoglobulin fusion proteins of the invention can be used as immunogens to produce antibodies in a subject, to purify ligands, and in screening assays to identify molecules that inhibit the interaction of a polypeptide of the invention with a ligand.

A chimeric or fusion protein of the invention can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, *e.g.*, by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers.

Alternatively, PCR amplification of gene fragments can be carried out using anchor primers that give rise to complementary overhangs between two consecutive gene fragments that can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for

example, Ausubel et al. (eds.) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley & Sons, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (*e.g.*, a GST polypeptide). A nucleic acid encoding a polypeptide of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the protein of the invention.

#### 4.8 GENE THERAPY

Mutations in the polynucleotides of the invention gene may result in loss of normal function of the encoded protein. The invention thus provides gene therapy to restore normal activity of the polypeptides of the invention; or to treat disease states involving polypeptides of the invention. Delivery of a functional gene encoding polypeptides of the invention to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (*e.g.*, adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (*e.g.*, liposomes or chemical treatments). See, for example, Anderson, Nature, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, Science, 244: 1275-1281 (1989); Verma, Scientific American: 68-84 (1990); and Miller, Nature, 357: 455-460 (1992). Introduction of any one of the nucleotides of the present invention or a gene encoding the polypeptides of the present invention can also be accomplished with extrachromosomal substrates (transient expression) or artificial chromosomes (stable expression). Cells may also be cultured *ex vivo* in the presence of proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes. Alternatively, it is contemplated that in other human disease states, preventing the expression of or inhibiting the activity of polypeptides of the invention will be useful in treating the disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of polypeptides of the invention.

Other methods inhibiting expression of a protein include the introduction of antisense molecules to the nucleic acids of the present invention, their complements, or their translated RNA sequences, by methods known in the art. Further, the polypeptides of the present invention can be inhibited by using targeted deletion methods, or the insertion of a negative regulatory element such as a silencer, which is tissue specific.

The present invention still further provides cells genetically engineered *in vivo* to express the polynucleotides of the invention, wherein such polynucleotides are in operative association with a regulatory sequence heterologous to the host cell which drives expression of the polynucleotides in



the cell. These methods can be used to increase or decrease the expression of the polynucleotides of the present invention.

Knowledge of DNA sequences provided by the invention allows for modification of cells to permit, increase, or decrease, expression of endogenous polypeptide. Cells can be modified (*e.g.*,  
5 by homologous recombination) to provide increased polypeptide expression by replacing, in whole or in part, the naturally occurring promoter with all or part of a heterologous promoter so that the cells express the protein at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to the desired protein encoding sequences. See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and  
10 PCT International Publication No. WO 91/09955. It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, *ada*, *dhfr*, and the multifunctional CAD gene which encodes carbamyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the desired protein coding sequence, amplification of the marker DNA by standard  
15 selection methods results in co-amplification of the desired protein coding sequences in the cells.

In another embodiment of the present invention, cells and tissues may be engineered to express an endogenous gene comprising the polynucleotides of the invention under the control of inducible regulatory elements, in which case the regulatory sequences of the endogenous gene may be replaced by homologous recombination. As described herein, gene targeting can be used to  
20 replace a gene's existing regulatory region with a regulatory sequence isolated from a different gene or a novel regulatory sequence synthesized by genetic engineering methods. Such regulatory sequences may be comprised of promoters, enhancers, scaffold-attachment regions, negative regulatory elements, transcriptional initiation sites, regulatory protein binding sites or combinations of said sequences. Alternatively, sequences which affect the structure or stability of the RNA or  
25 protein produced may be replaced, removed, added, or otherwise modified by targeting. These sequences include polyadenylation signals, mRNA stability elements, splice sites, leader sequences for enhancing or modifying transport or secretion properties of the protein, or other sequences which alter or improve the function or stability of protein or RNA molecules.

The targeting event may be a simple insertion of the regulatory sequence, placing the gene  
30 under the control of the new regulatory sequence, *e.g.*, inserting a new promoter or enhancer or both upstream of a gene. Alternatively, the targeting event may be a simple deletion of a regulatory element, such as the deletion of a tissue-specific negative regulatory element. Alternatively, the targeting event may replace an existing element; for example, a tissue-specific enhancer can be replaced by an enhancer that has broader or different cell-type specificity than the naturally  
35 occurring elements. Here, the naturally occurring sequences are deleted and new sequences are

added. In all cases, the identification of the targeting event may be facilitated by the use of one or more selectable marker genes that are contiguous with the targeting DNA, allowing for the selection of cells in which the exogenous DNA has integrated into the cell genome. The identification of the targeting event may also be facilitated by the use of one or more marker genes exhibiting the property of negative selection, such that the negatively selectable marker is linked to the exogenous DNA, but configured such that the negatively selectable marker flanks the targeting sequence, and such that a correct homologous recombination event with sequences in the host cell genome does not result in the stable integration of the negatively selectable marker. Markers useful for this purpose include the Herpes Simplex Virus thymidine kinase (TK) gene or the bacterial xanthine-guanine phosphoribosyl-transferase (gpt) gene.

The gene targeting or gene activation techniques which can be used in accordance with this aspect of the invention are more particularly described in U.S. Patent No. 5,272,071 to Chappel; U.S. Patent No. 5,578,461 to Sherwin et al.; International Application No. PCT/US92/09627 (WO93/09222) by Selden et al.; and International Application No. PCT/US90/06436 (WO91/06667) by Skoultchi et al., each of which is incorporated by reference herein in its entirety.

#### 4.9 TRANSGENIC ANIMALS

In preferred methods to determine biological functions of the polypeptides of the invention in vivo, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of a promoter of the polynucleotides of the invention is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The

homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

The polynucleotides of the present invention also make possible the development, through, *e.g.*, homologous recombination or knock out strategies, of animals that fail to express polypeptides of the invention or that express a variant polypeptide. Such animals are useful as models for studying the *in vivo* activities of polypeptide as well as for studying modulators of the polypeptides of the invention.

In preferred methods to determine biological functions of the polypeptides of the invention *in vivo*, one or more genes provided by the invention are either over expressed or inactivated in the germ line of animals using homologous recombination [Capecchi, Science 244:1288-1292 (1989)]. Animals in which the gene is over expressed, under the regulatory control of exogenous or endogenous promoter elements, are known as transgenic animals. Animals in which an endogenous gene has been inactivated by homologous recombination are referred to as "knockout" animals. Knockout animals, preferably non-human mammals, can be prepared as described in U.S. Patent No. 5,557,032, incorporated herein by reference. Transgenic animals are useful to determine the roles polypeptides of the invention play in biological processes, and preferably in disease states. Transgenic animals are useful as model systems to identify compounds that modulate lipid metabolism. Transgenic animals, preferably non-human mammals, are produced using methods as described in U.S. Patent No 5,489,743 and PCT Publication No. WO94/28122, incorporated herein by reference.

Transgenic animals can be prepared wherein all or part of the polynucleotides of the invention promoter is either activated or inactivated to alter the level of expression of the polypeptides of the invention. Inactivation can be carried out using homologous recombination methods described above. Activation can be achieved by supplementing or even replacing the homologous promoter to provide for increased protein expression. The homologous promoter can be supplemented by insertion of one or more heterologous enhancer elements known to confer promoter activation in a particular tissue.

#### 4.10 USES AND BIOLOGICAL ACTIVITY

The polynucleotides and proteins of the present invention are expected to exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified herein. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA). The mechanism underlying the particular condition or pathology will dictate whether the

polypeptides of the invention, the polynucleotides of the invention or modulators (activators or inhibitors) thereof would be beneficial to the subject in need of treatment. Thus, "therapeutic compositions of the invention" include compositions comprising isolated polynucleotides (including recombinant DNA molecules, cloned genes and degenerate variants thereof) or  
5 polypeptides of the invention (including full length protein, mature protein and truncations or domains thereof), or compounds and other substances that modulate the overall activity of the target gene products, either at the level of target gene/protein expression or target protein activity. Such modulators include polypeptides, analogs, (variants), including fragments and fusion proteins, antibodies and other binding proteins; chemical compounds that directly or  
10 indirectly activate or inhibit the polypeptides of the invention (identified, *e.g.*, via drug screening assays as described herein); antisense polynucleotides and polynucleotides suitable for triple helix formation; and in particular antibodies or other binding partners that specifically recognize one or more epitopes of the polypeptides of the invention.

The polypeptides of the present invention may likewise be involved in cellular activation  
15 or in one of the other physiological pathways described herein.

#### 4.10.1 RESEARCH USES AND UTILITIES

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant  
20 protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic  
25 disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as  
30 an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of  
35 the binding interaction.

The polypeptides provided by the present invention can similarly be used in assays to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding polypeptide is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

#### **4.10.2 NUTRITIONAL USES**

Polynucleotides and polypeptides of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the polypeptide or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the polypeptide or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

#### **4.10.3 CYTOKINE AND CELL PROLIFERATION/DIFFERENTIATION ACTIVITY**

A polypeptide of the present invention may exhibit activity relating to cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor-dependent cell proliferation assays, and hence the assays serve as a convenient

confirmation of cytokine activity. The activity of therapeutic compositions of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+(preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e, CMK,

5 HUVEC, and Caco. Therapeutic compositions of the invention can be used in the following:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in  
10 Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., I. Immunol. 149:3778-3783, 1992; Bowman et al., I. Immunol. 152:1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation,  
15 Kruisbeek, A. M. and Shevach, E. M. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human interleukin- $\gamma$ , Schreiber, R. D. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells  
20 include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L. S. and Lipsky, P. E. In Current Protocols in Immunology. J. E. e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse  
25 and human interleukin 6--Nordan, R. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11--Bennett, F., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin  
30 9--Ciarletta, A., Giannotti, J., Clark, S. C. and Turner, K. J. In Current Protocols in Immunology. J. E. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in  
35 Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W Strober,

Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, *In Vitro* assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### 4.10.4 STEM CELL GROWTH FACTOR ACTIVITY

A polypeptide of the present invention may exhibit stem cell growth factor activity and be involved in the proliferation, differentiation and survival of pluripotent and totipotent stem cells including primordial germ cells, embryonic stem cells, hematopoietic stem cells and/or germ line stem cells. Administration of the polypeptide of the invention to stem cells *in vivo* or *ex vivo* is expected to maintain and expand cell populations in a totipotent or pluripotent state which would be useful for re-engineering damaged or diseased tissues, transplantation, manufacture of bio-pharmaceuticals and the development of bio-sensors. The ability to produce large quantities of human cells has important working applications for the production of human proteins which currently must be obtained from non-human sources or donors, implantation of cells to treat diseases such as Parkinson's, Alzheimer's and other neurodegenerative diseases; tissues for grafting such as bone marrow, skin, cartilage, tendons, bone, muscle (including cardiac muscle), blood vessels, cornea, neural cells, gastrointestinal cells and others; and organs for transplantation such as kidney, liver, pancreas (including islet cells), heart and lung.

It is contemplated that multiple different exogenous growth factors and/or cytokines may be administered in combination with the polypeptide of the invention to achieve the desired effect, including any of the growth factors listed herein, other stem cell maintenance factors, and specifically including stem cell factor (SCF), leukemia inhibitory factor (LIF), Flt-3 ligand (Flt-3L), any of the interleukins, recombinant soluble IL-6 receptor fused to IL-6, macrophage inflammatory protein 1-alpha (MIP-1-alpha), G-CSF, GM-CSF, thrombopoietin (TPO), platelet factor 4 (PF-4), platelet-derived growth factor (PDGF), neural growth factors and basic fibroblast growth factor (bFGF).

Since totipotent stem cells can give rise to virtually any mature cell type, expansion of these cells in culture will facilitate the production of large quantities of mature cells. Techniques for culturing stem cells are known in the art and administration of polypeptides of the invention, optionally with other growth factors and/or cytokines, is expected to enhance the survival and proliferation of the stem cell populations. This can be accomplished by direct administration of the polypeptide of the invention to the culture medium. Alternatively, stroma cells transfected with a polynucleotide that encodes for the polypeptide of the invention can be used as a feeder

layer for the stem cell populations in culture or in vivo. Stromal support cells for feeder layers may include embryonic bone marrow fibroblasts, bone marrow stromal cells, fetal liver cells, or cultured embryonic fibroblasts (see U.S. Patent No. 5,690,926).

Stem cells themselves can be transfected with a polynucleotide of the invention to induce autocrine expression of the polypeptide of the invention. This will allow for generation of undifferentiated totipotent/pluripotent stem cell lines that are useful as is or that can then be differentiated into the desired mature cell types. These stable cell lines can also serve as a source of undifferentiated totipotent/pluripotent mRNA to create cDNA libraries and templates for polymerase chain reaction experiments. These studies would allow for the isolation and identification of differentially expressed genes in stem cell populations that regulate stem cell proliferation and/or maintenance.

Expansion and maintenance of totipotent stem cell populations will be useful in the treatment of many pathological conditions. For example, polypeptides of the present invention may be used to manipulate stem cells in culture to give rise to neuroepithelial cells that can be used to augment or replace cells damaged by illness, autoimmune disease, accidental damage or genetic disorders. The polypeptide of the invention may be useful for inducing the proliferation of neural cells and for the regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders which involve degeneration, death or trauma to neural cells or nerve tissue. In addition, the expanded stem cell populations can also be genetically altered for gene therapy purposes and to decrease host rejection of replacement tissues after grafting or implantation.

Expression of the polypeptide of the invention and its effect on stem cells can also be manipulated to achieve controlled differentiation of the stem cells into more differentiated cell types. A broadly applicable method of obtaining pure populations of a specific differentiated cell type from undifferentiated stem cell populations involves the use of a cell-type specific promoter driving a selectable marker. The selectable marker allows only cells of the desired type to survive. For example, stem cells can be induced to differentiate into cardiomyocytes (Wobus et al., *Differentiation*, 48: 173-182, (1991); Klug et al., *J. Clin. Invest.*, 98(1): 216-224, (1998)) or skeletal muscle cells (Browder, L. W. In: *Principles of Tissue Engineering* eds. Lanza et al., Academic Press (1997)). Alternatively, directed differentiation of stem cells can be accomplished by culturing the stem cells in the presence of a differentiation factor such as retinoic acid and an antagonist of the polypeptide of the invention which would inhibit the effects of endogenous stem cell factor activity and allow differentiation to proceed.

*In vitro* cultures of stem cells can be used to determine if the polypeptide of the invention exhibits stem cell growth factor activity. Stem cells are isolated from any one of various cell



sources (including hematopoietic stem cells and embryonic stem cells) and cultured on a feeder layer, as described by Thompson et al. Proc. Natl. Acad. Sci, U.S.A., 92: 7844-7848 (1995), in the presence of the polypeptide of the invention alone or in combination with other growth factors or cytokines. The ability of the polypeptide of the invention to induce stem cells proliferation is determined by colony formation on semi-solid support *e.g.* as described by Bernstein et al., Blood, 77: 2316-2321 (1991).

#### 4.10.5 HEMATOPOIESIS REGULATING ACTIVITY

A polypeptide of the present invention may be involved in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell disorders. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, *e.g.* in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (*i.e.*, traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either *in-vivo* or *ex-vivo* (*i.e.*, in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

Therapeutic compositions of the invention can be used in the following:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M. G. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, N.Y. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I. K. and Briddell, R. A. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, N.Y. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R. E. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, N.Y. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, N.Y. 1994; Long term culture initiating cell assay, Sutherland, H. J. In Culture of Hematopoietic Cells. R. I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, N.Y. 1994.

#### 4.10.6 TISSUE GROWTH ACTIVITY

A polypeptide of the present invention also may be involved in bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as in wound healing and tissue repair and replacement, and in healing of burns, incisions and ulcers.

A polypeptide of the present invention which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Compositions of a polypeptide, antibody, binding partner, or other modulator of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A polypeptide of this invention may also be involved in attracting bone-forming cells, stimulating growth of bone-forming cells, or inducing differentiation of progenitors of bone-forming cells. Treatment of osteoporosis, osteoarthritis, bone degenerative disorders, or periodontal disease, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes may also be possible using the composition of the invention.

Another category of tissue regeneration activity that may involve the polypeptide of the present invention is tendon/ligament formation. Induction of tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide environment to attract tendon- or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors *ex vivo* for return *in vivo* to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The compositions of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, *i.e.* for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a composition may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions that may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a composition of the invention.

Compositions of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

Compositions of the present invention may also be involved in the generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine,

kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring may allow normal tissue to regenerate. A polypeptide of the present invention may also exhibit angiogenic activity.

5 A composition of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A composition of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

10 Therapeutic compositions of the invention can be used in the following:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon); International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

15 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, H. I. and Rovee, D. T., eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### 20 4.10.7 IMMUNE STIMULATING OR SUPPRESSING ACTIVITY

A polypeptide of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A polynucleotide of the invention can encode a polypeptide exhibiting such activities. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), *e.g.*, in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (*e.g.*, HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpes viruses, mycobacteria, *Leishmania* spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, proteins of the present invention may also be useful where a boost to the immune system generally may be desirable, *i.e.*, in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein (or antagonists thereof, including antibodies) of the present invention may also to be useful in the treatment of allergic reactions and conditions (*e.g.*, anaphylaxis, serum sickness, drug reactions, food allergies, insect venom allergies, mastocytosis, allergic rhinitis, hypersensitivity pneumonitis, urticaria, angioedema, eczema, atopic dermatitis, allergic contact dermatitis, erythema multiforme, Stevens-Johnson syndrome, allergic conjunctivitis, atopic keratoconjunctivitis, venereal keratoconjunctivitis, giant papillary conjunctivitis and contact allergies), such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein (or antagonists thereof) of the present invention. The therapeutic effects of the polypeptides or antagonists thereof on allergic reactions can be evaluated by in vivo animals models such as the cumulative contact enhancement test (Lastbom et al., Toxicology 125: 59-66, 1998), skin prick test (Hoffmann et al., Allergy 54: 446-54, 1999), guinea pig skin sensitization test (Vohr et al., Arch. Toxicol. 73: 501-9), and murine local lymph node assay (Kimber et al., J. Toxicol. Environ. Health 53: 563-79).

Using the proteins of the invention it may also be possible to modulate immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as, for example, B7)), *e.g.*, preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue

transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a therapeutic composition of the invention may prevent cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, a lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular therapeutic compositions in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of therapeutic compositions of the invention on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self-tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block stimulation of T cells can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (e.g., a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune

responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response may be useful in cases of viral infection, including systemic viral diseases such as influenza, the common cold, and encephalitis.

5 Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected  
10 cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

A polypeptide of the present invention may provide the necessary stimulation signal to T  
15 cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient mounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (*e.g.*, a cytoplasmic-domain truncated portion) of an MHC class I alpha chain protein and  $\beta_2$  microglobulin protein or an MHC class II alpha chain  
20 protein and an MHC class II beta chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (*e.g.*, B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as  
25 the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the  
30 following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19;  
35 Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA

78:2488-2492, 1981; Herrmann et al., *J. Immunol.* 128:1968-1974, 1982; Handa et al., *J. Immunol.* 135:1564-1572, 1985; Takai et al., *J. Immunol.* 137:3494-3500, 1986; Takai et al., *J. Immunol.* 140:508-512, 1988; Bowman et al., *J. Virology* 61:1992-1998; Bertagnolli et al., *Cellular Immunology* 133:327-341, 1991; Brown et al., *J. Immunol.* 153:3079-3092, 1994.

- 5        Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. *Immunol.* 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J. J. and Brunswick, M. In *Current Protocols in Immunology*. J. E. e.a. Coligan eds. Vol 1  
10 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

- Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3,  
15 In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., *J. Immunol.* 137:3494-3500, 1986; Takai et al., *J. Immunol.* 140:508-512, 1988; Bertagnolli et al., *J. Immunol.* 149:3778-3783, 1992.

- Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in:  
20 Guery et al., *J. Immunol.* 134:536-544, 1995; Inaba et al., *Journal of Experimental Medicine* 173:549-559, 1991; Macatonia et al., *Journal of Immunology* 154:5071-5079, 1995; Porgador et al., *Journal of Experimental Medicine* 182:255-260, 1995; Nair et al., *Journal of Virology* 67:4062-4069, 1993; Huang et al., *Science* 264:961-965, 1994; Macatonia et al., *Journal of Experimental Medicine* 169:1255-1264, 1989; Bhardwaj et al., *Journal of Clinical Investigation*  
25 94:797-807, 1994; and Inaba et al., *Journal of Experimental Medicine* 172:631-640, 1990.

- Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., *Cytometry* 13:795-808, 1992; Gorczyca et al., *Leukemia* 7:659-670, 1993; Gorczyca et al., *Cancer Research*  
30 53:1945-1951, 1993; Itoh et al., *Cell* 66:233-243, 1991; Zacharchuk, *Journal of Immunology* 145:4037-4045, 1990; Zamai et al., *Cytometry* 14:891-897, 1993; Gorczyca et al., *International Journal of Oncology* 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., *Blood* 84:111-117, 1994; Fine et



al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

#### 4.10.8 ACTIVIN/INHIBIN ACTIVITY

5 A polypeptide of the present invention may also exhibit activin- or inhibin-related activities. A polynucleotide of the invention may encode a polypeptide exhibiting such characteristics. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a polypeptide of the present invention, 10 alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the polypeptide of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin group, may be useful as 15 a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, U.S. Pat. No. 4,798,885. A polypeptide of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as, but not limited to, cows, sheep and pigs.

20 The activity of a polypeptide of the invention may, among other means, be measured by the following methods.

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. 25 USA 83:3091-3095, 1986.

#### 4.10.9 CHEMOTACTIC/CHEMOKINETIC ACTIVITY

A polypeptide of the present invention may be involved in chemotactic or chemokinetic activity for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, 30 T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Chemotactic and chemokinetic receptor activation can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic compositions (*e.g.* proteins, antibodies, binding partners, or modulators of the invention) provide particular advantages in treatment of wounds and other 35 trauma to tissues, as well as in treatment of localized infections. For example, attraction of

lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population.

- 5 Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

Therapeutic compositions of the invention can be used in the following:

- 10 Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Marguiles, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates  
15 and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25:1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153:1762-1768, 1994.

#### 20           **4.10.10           HEMOSTATIC AND THROMBOLYTIC ACTIVITY**

- A polypeptide of the invention may also be involved in hemostasis or thrombolysis or thrombosis. A polynucleotide of the invention can encode a polypeptide exhibiting such attributes. Compositions may be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events  
25 in treating wounds resulting from trauma, surgery or other causes. A composition of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (*e.g.*, stroke).

Therapeutic compositions of the invention can be used in the following:

- 30 Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### 35           **4.10.11           CANCER DIAGNOSIS AND THERAPY**

Polypeptides of the invention may be involved in cancer cell generation, proliferation or metastasis. Detection of the presence or amount of polynucleotides or polypeptides of the invention may be useful for the diagnosis and/or prognosis of one or more types of cancer. For example, the presence or increased expression of a polynucleotide/polypeptide of the invention  
5 may indicate a hereditary risk of cancer, a precancerous condition, or an ongoing malignancy. Conversely, a defect in the gene or absence of the polypeptide may be associated with a cancer condition. Identification of single nucleotide polymorphisms associated with cancer or a predisposition to cancer may also be useful for diagnosis or prognosis.

Cancer treatments promote tumor regression by inhibiting tumor cell proliferation,  
10 inhibiting angiogenesis (growth of new blood vessels that is necessary to support tumor growth) and/or prohibiting metastasis by reducing tumor cell motility or invasiveness. Therapeutic compositions of the invention may be effective in adult and pediatric oncology including in solid phase tumors/malignancies, locally advanced tumors, human soft tissue sarcomas, metastatic cancer, including lymphatic metastases, blood cell malignancies including multiple myeloma,  
15 acute and chronic leukemias, and lymphomas, head and neck cancers including mouth cancer, larynx cancer and thyroid cancer, lung cancers including small cell carcinoma and non-small cell cancers, breast cancers including small cell carcinoma and ductal carcinoma, gastrointestinal cancers including esophageal cancer, stomach cancer, colon cancer, colorectal cancer and polyps associated with colorectal neoplasia, pancreatic cancers, liver cancer, urologic cancers including  
20 bladder cancer and prostate cancer, malignancies of the female genital tract including ovarian carcinoma, uterine (including endometrial) cancers, and solid tumor in the ovarian follicle, kidney cancers including renal cell carcinoma, brain cancers including intrinsic brain tumors, neuroblastoma, astrocytic brain tumors, gliomas, metastatic tumor cell invasion in the central nervous system, bone cancers including osteomas, skin cancers including malignant melanoma,  
25 tumor progression of human skin keratinocytes, squamous cell carcinoma, basal cell carcinoma, hemangiopericytoma and Kaposi's sarcoma.

Polypeptides, polynucleotides, or modulators of polypeptides of the invention (including inhibitors and stimulators of the biological activity of the polypeptide of the invention) may be administered to treat cancer. Therapeutic compositions can be administered in therapeutically  
30 effective dosages alone or in combination with adjuvant cancer therapy such as surgery, chemotherapy, radiotherapy, thermotherapy, and laser therapy, and may provide a beneficial effect, *e.g.* reducing tumor size, slowing rate of tumor growth, inhibiting metastasis, or otherwise improving overall clinical condition, without necessarily eradicating the cancer.

The composition can also be administered in therapeutically effective amounts as a  
35 portion of an anti-cancer cocktail. An anti-cancer cocktail is a mixture of the polypeptide or

modulator of the invention with one or more anti-cancer drugs in addition to a pharmaceutically acceptable carrier for delivery. The use of anti-cancer cocktails as a cancer treatment is routine. Anti-cancer drugs that are well known in the art and can be used as a treatment in combination with the polypeptide or modulator of the invention include: Actinomycin D,

5 Aminoglutethimide, Asparaginase, Bleomycin, Busulfan, Carboplatin, Carmustine, Chlorambucil, Cisplatin (cis-DDP), Cyclophosphamide, Cytarabine HCl (Cytosine arabinoside), Dacarbazine, Dactinomycin, Daunorubicin HCl, Doxorubicin HCl, Estramustine phosphate sodium, Etoposide (V16-213), Floxuridine, 5-Fluorouracil (5-Fu), Flutamide, Hydroxyurea (hydroxycarbamide), Ifosfamide, Interferon Alpha-2a, Interferon Alpha-2b, Leuprolide acetate  
10 (LHRH-releasing factor analog), Lomustine, Mechlorethamine HCl (nitrogen mustard), Melphalan, Mercaptopurine, Mesna, Methotrexate (MTX), Mitomycin, Mitoxantrone HCl, Octreotide, Plicamycin, Procarbazine HCl, Streptozocin, Tamoxifen citrate, Thioguanine, Thiotepa, Vinblastine sulfate, Vincristine sulfate, Amsacrine, Azacitidine, Hexamethylmelamine, Interleukin-2, Mitoguazone, Pentostatin, Semustine, Teniposide, and Vindesine sulfate.

15 In addition, therapeutic compositions of the invention may be used for prophylactic treatment of cancer. There are hereditary conditions and/or environmental situations (*e.g.* exposure to carcinogens) known in the art that predispose an individual to developing cancers. Under these circumstances, it may be beneficial to treat these individuals with therapeutically effective doses of the polypeptide of the invention to reduce the risk of developing cancers.

20 *In vitro* models can be used to determine the effective doses of the polypeptide of the invention as a potential cancer treatment. These *in vitro* models include proliferation assays of cultured tumor cells, growth of cultured tumor cells in soft agar (see Freshney, (1987) Culture of Animal Cells: A Manual of Basic Technique, Wiley-Liss, New York, NY Ch 18 and Ch 21), tumor systems in nude mice as described in Giovanella et al., J. Natl. Can. Inst., 52: 921-30  
25 (1974), mobility and invasive potential of tumor cells in Boyden Chamber assays as described in Pilkington et al., Anticancer Res., 17: 4107-9 (1997), and angiogenesis assays such as induction of vascularization of the chick chorioallantoic membrane or induction of vascular endothelial cell migration as described in Ribatta et al., Intl. J. Dev. Biol., 40: 1189-97 (1999) and Li et al., Clin. Exp. Metastasis, 17:423-9 (1999), respectively. Suitable tumor cells lines are available,  
30 *e.g.* from American Type Tissue Culture Collection catalogs.

#### 4.10.12 RECEPTOR/LIGAND ACTIVITY

A polypeptide of the present invention may also demonstrate activity as receptor, receptor ligand or inhibitor or agonist of receptor/ligand interactions. A polynucleotide of the  
35 invention can encode a polypeptide exhibiting such characteristics. Examples of such receptors

and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen  
5 recognition and development of cellular and humoral immune responses. Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

10 The activity of a polypeptide of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley- Interscience (Chapter 7.28,  
15 Measurement of Cellular Adhesion under static conditions 7.28.1- 7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

By way of example, the polypeptides of the invention may be used as a receptor for a  
20 ligand(s) thereby transmitting the biological activity of that ligand(s). Ligands may be identified through binding assays, affinity chromatography, dihybrid screening assays, BIAcore assays, gel overlay assays, or other methods known in the art.

Studies characterizing drugs or proteins as agonist or antagonist or partial agonists or a partial antagonist require the use of other proteins as competing ligands. The polypeptides of the  
25 present invention or ligand(s) thereof may be labeled by being coupled to radioisotopes, colorimetric molecules or toxin molecules by conventional methods. ("Guide to Protein Purification" Murray P. Deutscher (ed) Methods in Enzymology Vol. 182 (1990) Academic Press, Inc. San Diego). Examples of radioisotopes include, but are not limited to, tritium and carbon-14. Examples of colorimetric molecules include, but are not limited to, fluorescent  
30 molecules such as fluorescamine, or rhodamine or other colorimetric molecules. Examples of toxins include, but are not limited, to ricin.

#### 4.10.13 DRUG SCREENING

This invention is particularly useful for screening chemical compounds by using the  
35 novel polypeptides or binding fragments thereof in any of a variety of drug screening techniques.

The polypeptides or fragments employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the polypeptide or a fragment thereof. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between polypeptides of the invention or fragments and the agent being tested or examine the diminution in complex formation between the novel polypeptides and an appropriate cell line, which are well known in the art.

Sources for test compounds that may be screened for ability to bind to or modulate (*i.e.*, increase or decrease) the activity of polypeptides of the invention include (1) inorganic and organic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of either random or mimetic peptides, oligonucleotides or organic molecules.

Chemical libraries may be readily synthesized or purchased from a number of commercial sources, and may include structural analogs of known compounds or compounds that are identified as "hits" or "leads" via natural product screening.

The sources of natural product libraries are microorganisms (including bacteria and fungi), animals, plants or other vegetation, or marine organisms, and libraries of mixtures for screening may be created by: (1) fermentation and extraction of broths from soil, plant or marine microorganisms or (2) extraction of the organisms themselves. Natural product libraries include polyketides, non-ribosomal peptides, and (non-naturally occurring) variants thereof. For a review, see *Science* 282:63-68 (1998).

Combinatorial libraries are composed of large numbers of peptides, oligonucleotides or organic compounds and can be readily prepared by traditional automated synthesis methods, PCR, cloning or proprietary synthetic methods. Of particular interest are peptide and oligonucleotide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, *Curr. Opin. Biotechnol.* 8:701-707 (1997). For reviews and examples of peptidomimetic libraries, see Al-Obeidi et al., *Mol. Biotechnol.*, 9(3):205-23 (1998); Hruby et al., *Curr Opin Chem Biol*, 1(1):114-19 (1997); Dorner et al., *Bioorg Med Chem*, 4(5):709-15 (1996) (alkylated dipeptides).

Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to bind a polypeptide of the invention. The molecules identified in the binding assay are then tested for antagonist or agonist activity in *in vivo* tissue culture or animal models that are well known in the

art. In brief, the molecules are titrated into a plurality of cell cultures or animals and then tested for either cell/animal death or prolonged survival of the animal/cells.

The binding molecules thus identified may be complexed with toxins, *e.g.*, ricin or cholera, or with other compounds that are toxic to cells such as radioisotopes. The toxin-binding molecule complex is then targeted to a tumor or other cell by the specificity of the binding molecule for a polypeptide of the invention. Alternatively, the binding molecules may be complexed with imaging agents for targeting and imaging purposes.

#### 4.10.14 ASSAY FOR RECEPTOR ACTIVITY

The invention also provides methods to detect specific binding of a polypeptide *e.g.* a ligand or a receptor. The art provides numerous assays particularly useful for identifying previously unknown binding partners for receptor polypeptides of the invention. For example, expression cloning using mammalian or bacterial cells, or dihybrid screening assays can be used to identify polynucleotides encoding binding partners. As another example, affinity chromatography with the appropriate immobilized polypeptide of the invention can be used to isolate polypeptides that recognize and bind polypeptides of the invention. There are a number of different libraries used for the identification of compounds, and in particular small molecules, that modulate (*i.e.*, increase or decrease) biological activity of a polypeptide of the invention. Ligands for receptor polypeptides of the invention can also be identified by adding exogenous ligands, or cocktails of ligands to two cells populations that are genetically identical except for the expression of the receptor of the invention: one cell population expresses the receptor of the invention whereas the other does not. The responses of the two cell populations to the addition of ligands(s) are then compared. Alternatively, an expression library can be co-expressed with the polypeptide of the invention in cells and assayed for an autocrine response to identify potential ligand(s). As still another example, BIAcore assays, gel overlay assays, or other methods known in the art can be used to identify binding partner polypeptides, including, (1) organic and inorganic chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules.

The role of downstream intracellular signaling molecules in the signaling cascade of the polypeptide of the invention can be determined. For example, a chimeric protein in which the cytoplasmic domain of the polypeptide of the invention is fused to the extracellular portion of a protein, whose ligand has been identified, is produced in a host cell. The cell is then incubated with the ligand specific for the extracellular portion of the chimeric protein, thereby activating the chimeric receptor. Known downstream proteins involved in intracellular signaling can then

be assayed for expected modifications *i.e.* phosphorylation. Other methods known to those in the art can also be used to identify signaling molecules involved in receptor activity.

#### 4.10.15 ANTI-INFLAMMATORY ACTIVITY

5 Compositions of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production  
10 of other factors which more directly inhibit or promote an inflammatory response. Compositions with such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation intimation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or  
15 chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Compositions of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material. Compositions of this invention may be utilized to prevent or treat conditions such as, but not limited to, sepsis, acute pancreatitis, endotoxin shock, cytokine induced shock, rheumatoid  
20 arthritis, chronic inflammatory arthritis, pancreatic cell damage from diabetes mellitus type 1, graft versus host disease, inflammatory bowel disease, inflammation associated with pulmonary disease, other autoimmune disease or inflammatory disease, an antiproliferative agent such as for acute or chronic myelogenous leukemia or in the prevention of premature labor secondary to intrauterine infections.

#### 4.10.16 LEUKEMIAS

Leukemias and related disorders may be treated or prevented by administration of a therapeutic that promotes or inhibits function of the polynucleotides and/or polypeptides of the invention. Such leukemias and related disorders include but are not limited to acute leukemia,  
30 acute lymphocytic leukemia, acute myelocytic leukemia, myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia, chronic leukemia, chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia (for a review of such disorders, see Fishman et al., 1985, Medicine, 2d Ed., J.B. Lippincott Co., Philadelphia).

#### 4.10.17 NERVOUS SYSTEM DISORDERS



Nervous system disorders, involving cell types which can be tested for efficacy of intervention with compounds that modulate the activity of the polynucleotides and/or polypeptides of the invention, and which can be treated upon thus observing an indication of therapeutic utility, include but are not limited to nervous system injuries, and diseases or disorders which result in either a disconnection of axons, a diminution or degeneration of neurons, or demyelination. Nervous system lesions which may be treated in a patient (including human and non-human mammalian patients) according to the invention include but are not limited to the following lesions of either the central (including spinal cord, brain) or peripheral nervous systems:

(i) traumatic lesions, including lesions caused by physical injury or associated with surgery, for example, lesions which sever a portion of the nervous system, or compression injuries;

(ii) ischemic lesions, in which a lack of oxygen in a portion of the nervous system results in neuronal injury or death, including cerebral infarction or ischemia, or spinal cord infarction or ischemia;

(iii) infectious lesions, in which a portion of the nervous system is destroyed or injured as a result of infection, for example, by an abscess or associated with infection by human immunodeficiency virus, herpes zoster, or herpes simplex virus or with Lyme disease, tuberculosis, syphilis;

(iv) degenerative lesions, in which a portion of the nervous system is destroyed or injured as a result of a degenerative process including but not limited to degeneration associated with Parkinson's disease, Alzheimer's disease, Huntington's chorea, or amyotrophic lateral sclerosis;

(v) lesions associated with nutritional diseases or disorders, in which a portion of the nervous system is destroyed or injured by a nutritional disorder or disorder of metabolism including but not limited to, vitamin B12 deficiency, folic acid deficiency, Wernicke disease, tobacco-alcohol amblyopia, Marchiafava-Bignami disease (primary degeneration of the corpus callosum), and alcoholic cerebellar degeneration;

(vi) neurological lesions associated with systemic diseases including but not limited to diabetes (diabetic neuropathy, Bell's palsy), systemic lupus erythematosus, carcinoma, or sarcoidosis;

(vii) lesions caused by toxic substances including alcohol, lead, or particular neurotoxins; and

(viii) demyelinated lesions in which a portion of the nervous system is destroyed or injured by a demyelinating disease including but not limited to multiple sclerosis, human

immunodeficiency virus-associated myelopathy, transverse myelopathy or various etiologies, progressive multifocal leukoencephalopathy, and central pontine myelinolysis.

Therapeutics which are useful according to the invention for treatment of a nervous system disorder may be selected by testing for biological activity in promoting the survival or differentiation of neurons. For example, and not by way of limitation, therapeutics which elicit any of the following effects may be useful according to the invention:

- (i) increased survival time of neurons in culture;
- (ii) increased sprouting of neurons in culture or *in vivo*;
- (iii) increased production of a neuron-associated molecule in culture or *in vivo*, *e.g.*, choline acetyltransferase or acetylcholinesterase with respect to motor neurons; or
- (iv) decreased symptoms of neuron dysfunction *in vivo*.

Such effects may be measured by any method known in the art. In preferred, non-limiting embodiments, increased survival of neurons may be measured by the method set forth in Arakawa et al. (1990, J. Neurosci. 10:3507-3515); increased sprouting of neurons may be detected by methods set forth in Pestronk et al. (1980, Exp. Neurol. 70:65-82) or Brown et al. (1981, Ann. Rev. Neurosci. 4:17-42); increased production of neuron-associated molecules may be measured by bioassay, enzymatic assay, antibody binding, Northern blot assay, *etc.*, depending on the molecule to be measured; and motor neuron dysfunction may be measured by assessing the physical manifestation of motor neuron disorder, *e.g.*, weakness, motor neuron conduction velocity, or functional disability.

In specific embodiments, motor neuron disorders that may be treated according to the invention include but are not limited to disorders such as infarction, infection, exposure to toxin, trauma, surgical damage, degenerative disease or malignancy that may affect motor neurons as well as other components of the nervous system, as well as disorders that selectively affect neurons such as amyotrophic lateral sclerosis, and including but not limited to progressive spinal muscular atrophy, progressive bulbar palsy, primary lateral sclerosis, infantile and juvenile muscular atrophy, progressive bulbar paralysis of childhood (Fazio-Londe syndrome), poliomyelitis and the post polio syndrome, and Hereditary Motorsensory Neuropathy (Charcot-Marie-Tooth Disease).

#### 4.10.18 OTHER ACTIVITIES

A polypeptide of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye

color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or  
5 elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, co-factors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other  
10 than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or  
15 entity which is cross-reactive with such protein.

#### 4.10.19 IDENTIFICATION OF POLYMORPHISMS

The demonstration of polymorphisms makes possible the identification of such polymorphisms in human subjects and the pharmacogenetic use of this information for diagnosis  
20 and treatment. Such polymorphisms may be associated with, *e.g.*, differential predisposition or susceptibility to various disease states (such as disorders involving inflammation or immune response) or a differential response to drug administration, and this genetic information can be used to tailor preventive or therapeutic treatment appropriately. For example, the existence of a polymorphism associated with a predisposition to inflammation or autoimmune disease makes  
25 possible the diagnosis of this condition in humans by identifying the presence of the polymorphism.

Polymorphisms can be identified in a variety of ways known in the art which all generally involve obtaining a sample from a patient, analyzing DNA from the sample, optionally involving isolation or amplification of the DNA, and identifying the presence of the  
30 polymorphism in the DNA. For example, PCR may be used to amplify an appropriate fragment of genomic DNA which may then be sequenced. Alternatively, the DNA may be subjected to allele-specific oligonucleotide hybridization (in which appropriate oligonucleotides are hybridized to the DNA under conditions permitting detection of a single base mismatch) or to a single nucleotide extension assay (in which an oligonucleotide that hybridizes immediately  
35 adjacent to the position of the polymorphism is extended with one or more labeled nucleotides).

In addition, traditional restriction fragment length polymorphism analysis (using restriction enzymes that provide differential digestion of the genomic DNA depending on the presence or absence of the polymorphism) may be performed. Arrays with nucleotide sequences of the present invention can be used to detect polymorphisms. The array can comprise modified  
5 nucleotide sequences of the present invention in order to detect the nucleotide sequences of the present invention. In the alternative, any one of the nucleotide sequences of the present invention can be placed on the array to detect changes from those sequences.

Alternatively a polymorphism resulting in a change in the amino acid sequence could also be detected by detecting a corresponding change in amino acid sequence of the protein, *e.g.*,  
10 by an antibody specific to the variant sequence.

#### 4.10.20 ARTHRITIS AND INFLAMMATION

The immunosuppressive effects of the compositions of the invention against rheumatoid arthritis are determined in an experimental animal model system. The experimental model  
15 system is adjuvant induced arthritis in rats, and the protocol is described by J. Holoshitz, et al., 1983, Science, 219:56, or by B. Waksman et al., 1963, Int. Arch. Allergy Appl. Immunol., 23:129. Induction of the disease can be caused by a single injection, generally intradermally, of a suspension of killed Mycobacterium tuberculosis in complete Freund's adjuvant (CFA). The route of injection can vary, but rats may be injected at the base of the tail with an adjuvant  
20 mixture. The polypeptide is administered in phosphate buffered solution (PBS) at a dose of about 1-5 mg/kg. The control consists of administering PBS only.

The procedure for testing the effects of the test compound would consist of intradermally injecting killed Mycobacterium tuberculosis in CFA followed by immediately administering the test compound and subsequent treatment every other day until day 24. At 14, 15, 18, 20, 22, and  
25 24 days after injection of Mycobacterium CFA, an overall arthritis score may be obtained as described by J. Holoskitz above. An analysis of the data would reveal that the test compound would have a dramatic affect on the swelling of the joints as measured by a decrease of the arthritis score.

#### 4.11 THERAPEUTIC METHODS

The compositions (including polypeptide fragments, analogs, variants and antibodies or other binding partners or modulators including antisense polynucleotides) of the invention have numerous applications in a variety of therapeutic methods. Examples of therapeutic applications include, but are not limited to, those exemplified herein.

#### 4.11.1 EXAMPLE

One embodiment of the invention is the administration of an effective amount of the polypeptides or other composition of the invention to individuals affected by a disease or disorder that can be modulated by regulating the peptides of the invention. While the mode of administration is not particularly important, parenteral administration is preferred. An exemplary mode of administration is to deliver an intravenous bolus. The dosage of the polypeptides or other composition of the invention will normally be determined by the prescribing physician. It is to be expected that the dosage will vary according to the age, weight, condition and response of the individual patient. Typically, the amount of polypeptide administered per dose will be in the range of about 0.01 $\mu$ g/kg to 100 mg/kg of body weight, with the preferred dose being about 0.1 $\mu$ g/kg to 10 mg/kg of patient body weight. For parenteral administration, polypeptides of the invention will be formulated in an injectable form combined with a pharmaceutically acceptable parenteral vehicle. Such vehicles are well known in the art and examples include water, saline, Ringer's solution, dextrose solution, and solutions consisting of small amounts of the human serum albumin. The vehicle may contain minor amounts of additives that maintain the isotonicity and stability of the polypeptide or other active ingredient. The preparation of such solutions is within the skill of the art.

#### 4.12 PHARMACEUTICAL FORMULATIONS AND ROUTES OF ADMINISTRATION

A protein or other composition of the present invention (from whatever source derived, including without limitation from recombinant and non-recombinant sources and including antibodies and other binding partners of the polypeptides of the invention) may be administered to a patient in need, by itself, or in pharmaceutical compositions where it is mixed with suitable carriers or excipient(s) at doses to treat or ameliorate a variety of disorders. Such a composition may optionally contain (in addition to protein or other active ingredient and a carrier) diluents, fillers, salts, buffers, stabilizers, solubilizers, and other materials well known in the art. The term "pharmaceutically acceptable" means a non-toxic material that does not interfere with the effectiveness of the biological activity of the active ingredient(s). The characteristics of the carrier will depend on the route of administration. The pharmaceutical composition of the invention may also contain cytokines, lymphokines, or other hematopoietic factors such as M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IFN, TNF0, TNF1, TNF2, G-CSF, Meg-CSF, thrombopoietin, stem cell factor, and erythropoietin. In further compositions, proteins of the invention may be combined with other agents beneficial to the treatment of the disease or disorder in question. These agents

include various growth factors such as epidermal growth factor (EGF), platelet-derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), insulin-like growth factor (IGF), as well as cytokines described herein.

The pharmaceutical composition may further contain other agents which either enhance the activity of the protein or other active ingredient or complement its activity or use in treatment. Such additional factors and/or agents may be included in the pharmaceutical composition to produce a synergistic effect with protein or other active ingredient of the invention, or to minimize side effects. Conversely, protein or other active ingredient of the present invention may be included in formulations of the particular clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent to minimize side effects of the clotting factor, cytokine, lymphokine, other hematopoietic factor, thrombolytic or anti-thrombotic factor, or anti-inflammatory agent (such as IL-1Ra, IL-1 Hy1, IL-1 Hy2, anti-TNF, corticosteroids, immunosuppressive agents). A protein of the present invention may be active in multimers (*e.g.*, heterodimers or homodimers) or complexes with itself or other proteins. As a result, pharmaceutical compositions of the invention may comprise a protein of the invention in such multimeric or complexed form.

As an alternative to being included in a pharmaceutical composition of the invention including a first protein, a second protein or a therapeutic agent may be concurrently administered with the first protein (*e.g.*, at the same time, or at differing times provided that therapeutic concentrations of the combination of agents is achieved at the treatment site). Techniques for formulation and administration of the compounds of the instant application may be found in "Remington's Pharmaceutical Sciences," Mack Publishing Co., Easton, PA, latest edition. A therapeutically effective dose further refers to that amount of the compound sufficient to result in amelioration of symptoms, *e.g.*, treatment, healing, prevention or amelioration of the relevant medical condition, or an increase in rate of treatment, healing, prevention or amelioration of such conditions. When applied to an individual active ingredient, administered alone, a therapeutically effective dose refers to that ingredient alone. When applied to a combination, a therapeutically effective dose refers to combined amounts of the active ingredients that result in the therapeutic effect, whether administered in combination, serially or simultaneously.

In practicing the method of treatment or use of the present invention, a therapeutically effective amount of protein or other active ingredient of the present invention is administered to a mammal having a condition to be treated. Protein or other active ingredient of the present invention may be administered in accordance with the method of the invention either alone or in combination with other therapies such as treatments employing cytokines, lymphokines or other

hematopoietic factors. When co-administered with one or more cytokines, lymphokines or other hematopoietic factors, protein or other active ingredient of the present invention may be administered either simultaneously with the cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors, or sequentially. If administered sequentially, the attending physician will decide on the appropriate sequence of administering protein or other active ingredient of the present invention in combination with cytokine(s), lymphokine(s), other hematopoietic factor(s), thrombolytic or anti-thrombotic factors.

#### 4.12.1 ROUTES OF ADMINISTRATION

Suitable routes of administration may, for example, include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections. Administration of protein or other active ingredient of the present invention used in the pharmaceutical composition or to practice the method of the present invention can be carried out in a variety of conventional ways, such as oral ingestion, inhalation, topical application or cutaneous, subcutaneous, intraperitoneal, parenteral or intravenous injection. Intravenous administration to the patient is preferred.

Alternately, one may administer the compound in a local rather than systemic manner, for example, via injection of the compound directly into a arthritic joints or in fibrotic tissue, often in a depot or sustained release formulation. In order to prevent the scarring process frequently occurring as complication of glaucoma surgery, the compounds may be administered topically, for example, as eye drops. Furthermore, one may administer the drug in a targeted drug delivery system, for example, in a liposome coated with a specific antibody, targeting, for example, arthritic or fibrotic tissue. The liposomes will be targeted to and taken up selectively by the afflicted tissue.

The polypeptides of the invention are administered by any route that delivers an effective dosage to the desired site of action. The determination of a suitable route of administration and an effective dosage for a particular indication is within the level of skill in the art. Preferably for wound treatment, one administers the therapeutic compound directly to the site. Suitable dosage ranges for the polypeptides of the invention can be extrapolated from these dosages or from similar studies in appropriate animal models. Dosages can then be adjusted as necessary by the clinician to provide maximal therapeutic benefit.

#### 4.12.2 COMPOSITIONS/FORMULATIONS

Pharmaceutical compositions for use in accordance with the present invention thus may be formulated in a conventional manner using one or more physiologically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. These pharmaceutical compositions may be manufactured in a manner that is itself known, *e.g.*, by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes. Proper formulation is dependent upon the route of administration chosen. When a therapeutically effective amount of protein or other active ingredient of the present invention is administered orally, protein or other active ingredient of the present invention will be in the form of a tablet, capsule, powder, solution or elixir. When administered in tablet form, the pharmaceutical composition of the invention may additionally contain a solid carrier such as a gelatin or an adjuvant. The tablet, capsule, and powder contain from about 5 to 95% protein or other active ingredient of the present invention, and preferably from about 25 to 90% protein or other active ingredient of the present invention. When administered in liquid form, a liquid carrier such as water, petroleum, oils of animal or plant origin such as peanut oil, mineral oil, soybean oil, or sesame oil, or synthetic oils may be added. The liquid form of the pharmaceutical composition may further contain physiological saline solution, dextrose or other saccharide solution, or glycols such as ethylene glycol, propylene glycol or polyethylene glycol. When administered in liquid form, the pharmaceutical composition contains from about 0.5 to 90% by weight of protein or other active ingredient of the present invention, and preferably from about 1 to 50% protein or other active ingredient of the present invention.

When a therapeutically effective amount of protein or other active ingredient of the present invention is administered by intravenous, cutaneous or subcutaneous injection, protein or other active ingredient of the present invention will be in the form of a pyrogen-free, parenterally acceptable aqueous solution. The preparation of such parenterally acceptable protein or other active ingredient solutions, having due regard to pH, isotonicity, stability, and the like, is within the skill in the art. A preferred pharmaceutical composition for intravenous, cutaneous, or subcutaneous injection should contain, in addition to protein or other active ingredient of the present invention, an isotonic vehicle such as Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, Lactated Ringer's Injection, or other vehicle as known in the art. The pharmaceutical composition of the present invention may also contain stabilizers, preservatives, buffers, antioxidants, or other additives known to those of skill in the art. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks's solution, Ringer's solution, or physiological saline buffer. For transmucosal administration, penetrants appropriate



to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

For oral administration, the compounds can be formulated readily by combining the active compounds with pharmaceutically acceptable carriers well known in the art. Such carriers enable the compounds of the invention to be formulated as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. Pharmaceutical preparations for oral use can be obtained from a solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added. All formulations for oral administration should be in dosages suitable for such administration. For buccal administration, the compositions may take the form of tablets or lozenges formulated in conventional manner.

For administration by inhalation, the compounds for use according to the present invention are conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebuliser, with the use of a suitable propellant, *e.g.*, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges of, *e.g.*, gelatin for use

in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch. The compounds may be formulated for parenteral administration by injection, *e.g.*, by bolus injection or continuous infusion. Formulations for injection may be presented in unit dosage form, *e.g.*, in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions. Alternatively, the active ingredient may be in powder form for constitution with a suitable vehicle, *e.g.*, sterile pyrogen-free water, before use.

The compounds may also be formulated in rectal compositions such as suppositories or retention enemas, *e.g.*, containing conventional suppository bases such as cocoa butter or other glycerides. In addition to the formulations described previously, the compounds may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

A pharmaceutical carrier for the hydrophobic compounds of the invention is a co-solvent system comprising benzyl alcohol, a nonpolar surfactant, a water-miscible organic polymer, and an aqueous phase. The co-solvent system may be the VPD co-solvent system. VPD is a solution of 3% w/v benzyl alcohol, 8% w/v of the nonpolar surfactant polysorbate 80, and 65% w/v polyethylene glycol 300, made up to volume in absolute ethanol. The VPD co-solvent system (VPD:5W) consists of VPD diluted 1:1 with a 5% dextrose in water solution. This co-solvent system dissolves hydrophobic compounds well, and itself produces low toxicity upon systemic administration. Naturally, the proportions of a co-solvent system may be varied considerably without destroying its solubility and toxicity characteristics. Furthermore, the identity of the co-solvent components may be varied: for example, other low-toxicity nonpolar surfactants may

be used instead of polysorbate 80; the fraction size of polyethylene glycol may be varied; other biocompatible polymers may replace polyethylene glycol, *e.g.* polyvinyl pyrrolidone; and other sugars or polysaccharides may substitute for dextrose. Alternatively, other delivery systems for hydrophobic pharmaceutical compounds may be employed. Liposomes and emulsions are well known examples of delivery vehicles or carriers for hydrophobic drugs. Certain organic solvents such as dimethylsulfoxide also may be employed, although usually at the cost of greater toxicity. Additionally, the compounds may be delivered using a sustained-release system, such as semipermeable matrices of solid hydrophobic polymers containing the therapeutic agent. Various types of sustained-release materials have been established and are well known by those skilled in the art. Sustained-release capsules may, depending on their chemical nature, release the compounds for a few weeks up to over 100 days. Depending on the chemical nature and the biological stability of the therapeutic reagent, additional strategies for protein or other active ingredient stabilization may be employed.

The pharmaceutical compositions also may comprise suitable solid or gel phase carriers or excipients. Examples of such carriers or excipients include but are not limited to calcium carbonate, calcium phosphate, various sugars, starches, cellulose derivatives, gelatin, and polymers such as polyethylene glycols. Many of the active ingredients of the invention may be provided as salts with pharmaceutically compatible counter ions. Such pharmaceutically acceptable base addition salts are those salts which retain the biological effectiveness and properties of the free acids and which are obtained by reaction with inorganic or organic bases such as sodium hydroxide, magnesium hydroxide, ammonia, trialkylamine, dialkylamine, monoalkylamine, dibasic amino acids, sodium acetate, potassium benzoate, triethanol amine and the like.

The pharmaceutical composition of the invention may be in the form of a complex of the protein(s) or other active ingredient(s) of present invention along with protein or peptide antigens. The protein and/or peptide antigen will deliver a stimulatory signal to both B and T lymphocytes. B-lymphocytes will respond to antigen through their surface immunoglobulin receptor. T lymphocytes will respond to antigen through the T cell receptor (TCR) following presentation of the antigen by MHC proteins. MHC and structurally related proteins including those encoded by class I and class II MHC genes on host cells will serve to present the peptide antigen(s) to T lymphocytes. The antigen components could also be supplied as purified MHC-peptide complexes alone or with co-stimulatory molecules that can directly signal T cells. Alternatively antibodies able to bind surface immunoglobulin and other molecules on B cells as well as antibodies able to bind the TCR and other molecules on T cells can be combined with the pharmaceutical composition of the invention.

The pharmaceutical composition of the invention may be in the form of a liposome in which protein of the present invention is combined, in addition to other pharmaceutically acceptable carriers, with amphipathic agents such as lipids which exist in aggregated form as micelles, insoluble monolayers, liquid crystals, or lamellar layers in aqueous solution. Suitable lipids for liposomal formulation include, without limitation, monoglycerides, diglycerides, sulfatides, lysolecithins, phospholipids, saponin, bile acids, and the like. Preparation of such liposomal formulations is within the level of skill in the art, as disclosed, for example, in U.S. Patent Nos. 4,235,871; 4,501,728; 4,837,028; and 4,737,323, all of which are incorporated herein by reference.

The amount of protein or other active ingredient of the present invention in the pharmaceutical composition of the present invention will depend upon the nature and severity of the condition being treated, and on the nature of prior treatments which the patient has undergone. Ultimately, the attending physician will decide the amount of protein or other active ingredient of the present invention with which to treat each individual patient. Initially, the attending physician will administer low doses of protein or other active ingredient of the present invention and observe the patient's response. Larger doses of protein or other active ingredient of the present invention may be administered until the optimal therapeutic effect is obtained for the patient, and at that point the dosage is not increased further. It is contemplated that the various pharmaceutical compositions used to practice the method of the present invention should contain about 0.01  $\mu\text{g}$  to about 100 mg (preferably about 0.1  $\mu\text{g}$  to about 10 mg, more preferably about 0.1  $\mu\text{g}$  to about 1 mg) of protein or other active ingredient of the present invention per kg body weight. For compositions of the present invention which are useful for bone, cartilage, tendon or ligament regeneration, the therapeutic method includes administering the composition topically, systematically, or locally as an implant or device. When administered, the therapeutic composition for use in this invention is, of course, in a pyrogen-free, physiologically acceptable form. Further, the composition may desirably be encapsulated or injected in a viscous form for delivery to the site of bone, cartilage or tissue damage. Topical administration may be suitable for wound healing and tissue repair. Therapeutically useful agents other than a protein or other active ingredient of the invention which may also optionally be included in the composition as described above, may alternatively or additionally, be administered simultaneously or sequentially with the composition in the methods of the invention. Preferably for bone and/or cartilage formation, the composition would include a matrix capable of delivering the protein-containing or other active ingredient-containing composition to the site of bone and/or cartilage damage, providing a structure for the developing bone and cartilage and optimally

capable of being resorbed into the body. Such matrices may be formed of materials presently in use for other implanted medical applications.

The choice of matrix material is based on biocompatibility, biodegradability, mechanical properties, cosmetic appearance and interface properties. The particular application of the compositions will define the appropriate formulation. Potential matrices for the compositions may be biodegradable and chemically defined calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyglycolic acid and polyanhydrides. Other potential materials are biodegradable and biologically well-defined, such as bone or dermal collagen. Further matrices are comprised of pure proteins or extracellular matrix components. Other potential matrices are nonbiodegradable and chemically defined, such as sintered hydroxyapatite, bioglass, aluminates, or other ceramics. Matrices may be comprised of combinations of any of the above-mentioned types of material, such as polylactic acid and hydroxyapatite or collagen and tricalcium phosphate. The bioceramics may be altered in composition, such as in calcium-aluminate-phosphate and processing to alter pore size, particle size, particle shape, and biodegradability. Presently preferred is a 50:50 (mole weight) copolymer of lactic acid and glycolic acid in the form of porous particles having diameters ranging from 150 to 800 microns. In some applications, it will be useful to utilize a sequestering agent, such as carboxymethyl cellulose or autologous blood clot, to prevent the protein compositions from disassociating from the matrix.

A preferred family of sequestering agents is cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), including methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropyl-methylcellulose, and carboxymethylcellulose, the most preferred being cationic salts of carboxymethylcellulose (CMC). Other preferred sequestering agents include hyaluronic acid, sodium alginate, poly(ethylene glycol), polyoxyethylene oxide, carboxyvinyl polymer and poly(vinyl alcohol). The amount of sequestering agent useful herein is 0.5-20 wt %, preferably 1-10 wt % based on total formulation weight, which represents the amount necessary to prevent desorption of the protein from the polymer matrix and to provide appropriate handling of the composition, yet not so much that the progenitor cells are prevented from infiltrating the matrix, thereby providing the protein the opportunity to assist the osteogenic activity of the progenitor cells. In further compositions, proteins or other active ingredients of the invention may be combined with other agents beneficial to the treatment of the bone and/or cartilage defect, wound, or tissue in question. These agents include various growth factors such as epidermal growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factors (TGF- $\alpha$  and TGF- $\beta$ ), and insulin-like growth factor (IGF).

The therapeutic compositions are also presently valuable for veterinary applications. Particularly domestic animals and thoroughbred horses, in addition to humans, are desired patients for such treatment with proteins or other active ingredients of the present invention. The dosage regimen of a protein-containing pharmaceutical composition to be used in tissue  
5 regeneration will be determined by the attending physician considering various factors which modify the action of the proteins, *e.g.*, amount of tissue weight desired to be formed, the site of damage, the condition of the damaged tissue, the size of a wound, type of damaged tissue (*e.g.*, bone), the patient's age, sex, and diet, the severity of any infection, time of administration and other clinical factors. The dosage may vary with the type of matrix used in the reconstitution  
10 and with inclusion of other proteins in the pharmaceutical composition. For example, the addition of other known growth factors, such as IGF I (insulin like growth factor I), to the final composition, may also effect the dosage. Progress can be monitored by periodic assessment of tissue/bone growth and/or repair, for example, X-rays, histomorphometric determinations and tetracycline labeling.

15 Polynucleotides of the present invention can also be used for gene therapy. Such polynucleotides can be introduced either *in vivo* or *ex vivo* into cells for expression in a mammalian subject. Polynucleotides of the invention may also be administered by other known methods for introduction of nucleic acid into a cell or organism (including, without limitation, in the form of viral vectors or naked DNA). Cells may also be cultured *ex vivo* in the presence of  
20 proteins of the present invention in order to proliferate or to produce a desired effect on or activity in such cells. Treated cells can then be introduced *in vivo* for therapeutic purposes.

#### 4.12.3 EFFECTIVE DOSAGE

Pharmaceutical compositions suitable for use in the present invention include  
25 compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. More specifically, a therapeutically effective amount means an amount effective to prevent development of or to alleviate the existing symptoms of the subject being treated. Determination of the effective amount is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein. For any compound used in  
30 the method of the invention, the therapeutically effective dose can be estimated initially from appropriate *in vitro* assays. For example, a dose can be formulated in animal models to achieve a circulating concentration range that can be used to more accurately determine useful doses in humans. For example, a dose can be formulated in animal models to achieve a circulating concentration range that includes the  $IC_{50}$  as determined in cell culture (*i.e.*, the concentration of

the test compound which achieves a half-maximal inhibition of the protein's biological activity). Such information can be used to more accurately determine useful doses in humans.

A therapeutically effective dose refers to that amount of the compound that results in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, *e.g.*, for determining the LD<sub>50</sub> (the dose lethal to 50% of the population) and the ED<sub>50</sub> (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio between LD<sub>50</sub> and ED<sub>50</sub>. Compounds which exhibit high therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in human. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED<sub>50</sub> with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. See, *e.g.*, Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p.1. Dosage amount and interval may be adjusted individually to provide plasma levels of the active moiety which are sufficient to maintain the desired effects, or minimal effective concentration (MEC). The MEC will vary for each compound but can be estimated from *in vitro* data. Dosages necessary to achieve the MEC will depend on individual characteristics and route of administration. However, HPLC assays or bioassays can be used to determine plasma concentrations.

Dosage intervals can also be determined using MEC value. Compounds should be administered using a regimen that maintains plasma levels above the MEC for 10-90% of the time, preferably between 30-90% and most preferably between 50-90%. In cases of local administration or selective uptake, the effective local concentration of the drug may not be related to plasma concentration.

An exemplary dosage regimen for polypeptides or other compositions of the invention will be in the range of about 0.01 µg/kg to 100 mg/kg of body weight daily, with the preferred dose being about 0.1 µg/kg to 25 mg/kg of patient body weight daily, varying in adults and children. Dosing may be once daily, or equivalent doses may be delivered at longer or shorter intervals.

The amount of composition administered will, of course, be dependent on the subject being treated, on the subject's age and weight, the severity of the affliction, the manner of administration and the judgment of the prescribing physician.

#### 4.12.4 PACKAGING

The compositions may, if desired, be presented in a pack or dispenser device which may contain one or more unit dosage forms containing the active ingredient. The pack may, for example, comprise metal or plastic foil, such as a blister pack. The pack or dispenser device may be accompanied by instructions for administration. Compositions comprising a compound of the invention formulated in a compatible pharmaceutical carrier may also be prepared, placed in an appropriate container, and labeled for treatment of an indicated condition.

#### 4.13 ANTIBODIES

Also included in the invention are antibodies to proteins, or fragments of proteins of the invention. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of immunoglobulin (Ig) molecules, *i.e.*, molecules that contain an antigen-binding site that specifically binds (immunoreacts with) an antigen. Such antibodies include, but are not limited to, polyclonal, monoclonal, chimeric, single chain,  $F_{ab}$ ,  $F_{ab}'$ , and  $F_{(ab)2}$  fragments, and an  $F_{ab}$  expression library. In general, an antibody molecule obtained from humans relates to any of the classes IgG, IgM, IgA, IgE and IgD, which differ from one another by the nature of the heavy chain present in the molecule. Certain classes have subclasses as well, such as IgG<sub>1</sub>, IgG<sub>2</sub>, and others. Furthermore, in humans, the light chain may be a kappa chain or a lambda chain. Reference herein to antibodies includes a reference to all such classes, subclasses and types of human antibody species.

An isolated related protein of the invention may be intended to serve as an antigen, or a portion or fragment thereof, and additionally can be used as an immunogen to generate antibodies that immunospecifically bind the antigen, using standard techniques for polyclonal and monoclonal antibody preparation. The full-length protein can be used or, alternatively, the invention provides antigenic peptide fragments of the antigen for use as immunogens. An antigenic peptide fragment comprises at least 6 amino acid residues of the amino acid sequence of any of the full length proteins of the invention, and encompasses an epitope thereof such that an antibody raised against the peptide forms a specific immune complex with the full length protein or with any fragment that contains the epitope. Preferably, the antigenic peptide comprises at least 10 amino acid residues, or at least 15 amino acid residues, or at least 20 amino acid residues, or at least 30 amino acid residues. Preferred epitopes encompassed by the antigenic peptide are regions of the protein that are located on its surface; commonly these are hydrophilic regions.

In certain embodiments of the invention, at least one epitope encompassed by the antigenic peptide is a region on the surface of the protein of the invention, *e.g.*, a hydrophilic



region. A hydrophobicity analysis of the human related protein sequence will indicate which regions of a related protein are particularly hydrophilic and, therefore, are likely to encode surface residues useful for targeting antibody production. As a means for targeting antibody production, hydropathy plots showing regions of hydrophilicity and hydrophobicity may be generated by any method well known in the art, including, for example, the Kyte Doolittle or the Hopp Woods methods, either with or without Fourier transformation. See, *e.g.*, Hopp and Woods, 1981, *Proc. Nat. Acad. Sci. USA* 78: 3824-3828; Kyte and Doolittle 1982, *J. Mol. Biol.* 157: 105-142, each of which is incorporated herein by reference in its entirety. Antibodies that are specific for one or more domains within an antigenic protein, or derivatives, fragments, analogs or homologs thereof, are also provided herein.

A protein of the invention, or a derivative, fragment, analog, homolog or ortholog thereof, may be utilized as an immunogen in the generation of antibodies that immunospecifically bind these protein components.

Various procedures known within the art may be used for the production of polyclonal or monoclonal antibodies directed against a protein of the invention, or against derivatives, fragments, analogs homologs or orthologs thereof (see, for example, *Antibodies: A Laboratory Manual*, Harlow E, and Lane D, 1988, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, incorporated herein by reference). Some of these antibodies are discussed below.

### 5.13.1 Polyclonal Antibodies

For the production of polyclonal antibodies, various suitable host animals (*e.g.*, rabbit, goat, mouse or other mammal) may be immunized by one or more injections with the native protein, a synthetic variant thereof, or a derivative of the foregoing. An appropriate immunogenic preparation can contain, for example, the naturally occurring immunogenic protein, a chemically synthesized polypeptide representing the immunogenic protein, or a recombinantly expressed immunogenic protein. Furthermore, the protein may be conjugated to a second protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. The preparation can further include an adjuvant. Various adjuvants used to increase the immunological response include, but are not limited to, Freund's (complete and incomplete), mineral gels (*e.g.*, aluminum hydroxide), surface active substances (*e.g.*, lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, dinitrophenol, etc.), adjuvants usable in humans such as Bacille Calmette-Guerin and *Corynebacterium parvum*, or similar immunostimulatory agents. Additional examples of

adjuvants which can be employed include MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

The polyclonal antibody molecules directed against the immunogenic protein can be isolated from the mammal (*e.g.*, from the blood) and further purified by well known techniques, such as affinity chromatography using protein A or protein G, which provide primarily the IgG fraction of immune serum. Subsequently, or alternatively, the specific antigen which is the target of the immunoglobulin sought, or an epitope thereof, may be immobilized on a column to purify the immune specific antibody by immunoaffinity chromatography. Purification of immunoglobulins is discussed, for example, by D. Wilkinson (*The Scientist*, published by The Scientist, Inc., Philadelphia PA, Vol. 14, No. 8 (April 17, 2000), pp. 25-28).

### 5.13.2 Monoclonal Antibodies

The term "monoclonal antibody" (MAb) or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one molecular species of antibody molecule consisting of a unique light chain gene product and a unique heavy chain gene product. In particular, the complementarity determining regions (CDRs) of the monoclonal antibody are identical in all the molecules of the population. MAbs thus contain an antigen-binding site capable of immunoreacting with a particular epitope of the antigen characterized by a unique binding affinity for it.

Monoclonal antibodies can be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes can be immunized in vitro.

The immunizing agent will typically include the protein antigen, a fragment thereof or a fusion protein thereof. Generally, either peripheral blood lymphocytes are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (Goding, *Monoclonal Antibodies: Principles and Practice*, Academic Press, (1986) pp. 59-103). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells can be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the

culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies (Kozbor, *J. Immunol.*, **133**:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63).

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the antigen. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, *Anal. Biochem.*, **107**:220 (1980). Preferably, antibodies having a high degree of specificity and a high binding affinity for the target antigen are isolated.

After the desired hybridoma cells are identified, the clones can be subcloned by limiting dilution procedures and grown by standard methods. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells can be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclones can be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies can also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA can be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or

myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also can be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences (U.S. Patent No. 4,816,567; Morrison, Nature 368, 812-13 (1994)) or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

### 5.13.2 Humanized Antibodies

The antibodies directed against the protein antigens of the invention can further comprise humanized antibodies or human antibodies. These antibodies are suitable for administration to humans without engendering an immune response by the human against the administered immunoglobulin. Humanized forms of antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')<sub>2</sub> or other antigen-binding subsequences of antibodies) that are principally comprised of the sequence of a human immunoglobulin, and contain minimal sequence derived from a non-human immunoglobulin. Humanization can be performed following the method of Winter and co-workers (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. (See also U.S. Patent No. 5,225,539.) In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies can also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., 1986; Riechmann et al., 1988; and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

### 5.13.3 Human Antibodies

Fully human antibodies relate to antibody molecules in which essentially the entire sequences of both the light chain and the heavy chain, including the CDRs, arise from human genes. Such antibodies are termed "human antibodies", or "fully human antibodies" herein. Human monoclonal antibodies can be prepared by the trioma technique; the human B-cell hybridoma technique (see Kozbor, et al., 1983 Immunol Today 4: 72) and the EBV hybridoma technique to produce human monoclonal antibodies (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96). Human monoclonal antibodies may be utilized in the practice of the present invention and may be produced by using human hybridomas (see Cote, et al., 1983. Proc Natl Acad Sci USA 80: 2026-2030) or by transforming human B-cells with Epstein Barr Virus in vitro (see Cole, et al., 1985 In: MONOCLONAL ANTIBODIES AND CANCER THERAPY, Alan R. Liss, Inc., pp. 77-96).

In addition, human antibodies can also be produced using additional techniques, including phage display libraries (Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)). Similarly, human antibodies can be made by introducing human immunoglobulin loci into transgenic animals, *e.g.*, mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in Marks et al. (Bio/Technology 10, 779-783 (1992)); Lonberg et al. (Nature 368 856-859 (1994)); Morrison ( Nature 368, 812-13 (1994)); Fishwild et al.,( Nature Biotechnology 14, 845-51 (1996)); Neuberger (Nature Biotechnology 14, 826 (1996)); and Lonberg and Huszar (Intern. Rev. Immunol. 13 65-93 (1995)).

Human antibodies may additionally be produced using transgenic nonhuman animals which are modified so as to produce fully human antibodies rather than the animal's endogenous antibodies in response to challenge by an antigen. (See PCT publication WO94/02602). The endogenous genes encoding the heavy and light immunoglobulin chains in the nonhuman host have been incapacitated, and active loci encoding human heavy and light chain immunoglobulins are inserted into the host's genome. The human genes are incorporated, for example, using yeast artificial chromosomes containing the requisite human DNA segments. An animal which provides all the desired modifications is then obtained as progeny by crossbreeding intermediate transgenic animals containing fewer than the full complement of the modifications. The preferred embodiment of such a nonhuman animal is a mouse, and is termed the Xenomouse<sup>TM</sup> as disclosed in PCT publications WO 96/33735 and WO 96/34096. This animal produces B cells which secrete fully human immunoglobulins. The antibodies can be obtained directly from

the animal after immunization with an immunogen of interest, as, for example, a preparation of a polyclonal antibody, or alternatively from immortalized B cells derived from the animal, such as hybridomas producing monoclonal antibodies. Additionally, the genes encoding the immunoglobulins with human variable regions can be recovered and expressed to obtain the antibodies directly, or can be further modified to obtain analogs of antibodies such as, for example, single chain Fv molecules.

An example of a method of producing a nonhuman host, exemplified as a mouse, lacking expression of an endogenous immunoglobulin heavy chain is disclosed in U.S. Patent No. 5,939,598. It can be obtained by a method including deleting the J segment genes from at least one endogenous heavy chain locus in an embryonic stem cell to prevent rearrangement of the locus and to prevent formation of a transcript of a rearranged immunoglobulin heavy chain locus, the deletion being effected by a targeting vector containing a gene encoding a selectable marker; and producing from the embryonic stem cell a transgenic mouse whose somatic and germ cells contain the gene encoding the selectable marker.

A method for producing an antibody of interest, such as a human antibody, is disclosed in U.S. Patent No. 5,916,771. It includes introducing an expression vector that contains a nucleotide sequence encoding a heavy chain into one mammalian host cell in culture, introducing an expression vector containing a nucleotide sequence encoding a light chain into another mammalian host cell, and fusing the two cells to form a hybrid cell. The hybrid cell expresses an antibody containing the heavy chain and the light chain.

In a further improvement on this procedure, a method for identifying a clinically relevant epitope on an immunogen, and a correlative method for selecting an antibody that binds immunospecifically to the relevant epitope with high affinity, are disclosed in PCT publication WO 99/53049.

#### 5.13.4 F<sub>ab</sub> Fragments and Single Chain Antibodies

According to the invention, techniques can be adapted for the production of single-chain antibodies specific to an antigenic protein of the invention (see *e.g.*, U.S. Patent No. 4,946,778). In addition, methods can be adapted for the construction of F<sub>ab</sub> expression libraries (see *e.g.*, Huse, et al., 1989 Science 246: 1275-1281) to allow rapid and effective identification of monoclonal F<sub>ab</sub> fragments with the desired specificity for a protein or derivatives, fragments, analogs or homologs thereof. Antibody fragments that contain the idiotypes to a protein antigen may be produced by techniques known in the art including, but not limited to: (i) an F<sub>(ab')<sub>2</sub></sub> fragment produced by pepsin digestion of an antibody molecule; (ii) an F<sub>ab</sub> fragment generated

by reducing the disulfide bridges of an  $F_{(ab)2}$  fragment; (iii) an  $F_{ab}$  fragment generated by the treatment of the antibody molecule with papain and a reducing agent and (iv)  $F_v$  fragments.

### 5.13.5 Bispecific Antibodies

5 Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for an antigenic protein of the invention. The second binding target is any other antigen, and advantageously is a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the  
10 recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities (Milstein and Cuello, *Nature*, 305:537-539 (1983)). Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct  
15 bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, 1991 *EMBO J.*, 10:3655-3659.

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion  
20 preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable  
25 host organism. For further details of generating bispecific antibodies see, for example, Suresh *et al.*, *Methods in Enzymology*, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the  
30 CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (*e.g.* tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large amino acid side chains with smaller ones (*e.g.* alanine or threonine). This provides a mechanism for  
35 increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (*e.g.* F(ab')<sub>2</sub> bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')<sub>2</sub> fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Additionally, Fab' fragments can be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby et al., J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')<sub>2</sub> molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected to directed chemical coupling in vitro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various techniques for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers. Kostelny et al., J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V<sub>H</sub>) connected to a light-chain variable domain (V<sub>L</sub>) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V<sub>H</sub> and V<sub>L</sub> domains of one fragment are forced to pair with the complementary V<sub>L</sub> and V<sub>H</sub> domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber et al., J. Immunol. 152:5368 (1994).



Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt et al., *J. Immunol.* 147:60 (1991).

Exemplary bispecific antibodies can bind to two different epitopes, at least one of which originates in the protein antigen of the invention. Alternatively, an anti-antigenic arm of an immunoglobulin molecule can be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (*e.g.* CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular antigen. Bispecific antibodies can also be used to direct cytotoxic agents to cells which express a particular antigen. These antibodies possess an antigen-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the protein antigen described herein and further binds tissue factor (TF).

#### 5.13.6 Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells (U.S. Patent No. 4,676,980), and for treatment of HIV infection (WO 91/00360; WO 92/200373; EP 03089). It is contemplated that the antibodies can be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins can be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

#### 5.13.7 Effector Function Engineering

It can be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, *e.g.*, the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) can be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated can have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., *J. Exp Med.*, 176: 1191-1195 (1992) and Shopes, *J. Immunol.*, 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity can also be prepared using heterobifunctional cross-linkers as described in Wolff et al. *Cancer Research*, 53: 2560-2565 (1993). Alternatively, an antibody can

be engineered that has dual Fc regions and can thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., *Anti-Cancer Drug Design*, 3: 219-230 (1989).

### 5.13.8 Immunoconjugates

5 The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been  
10 described above. Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin,  
15 mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated antibodies. Examples include  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP),  
20 iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a  
25 ricin immunotoxin can be prepared as described in Vitetta et al., *Science*, 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

In another embodiment, the antibody can be conjugated to a "receptor" (such  
30 streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is in turn conjugated to a cytotoxic agent.

## 35 4.14 COMPUTER READABLE SEQUENCES

In one application of this embodiment, a nucleotide sequence of the present invention can be recorded on computer readable media. As used herein, "computer readable media" refers to any medium which can be read and accessed directly by a computer. Such media include, but are not limited to: magnetic storage media, such as floppy discs, hard disc storage medium, and magnetic tape; optical storage media such as CD-ROM; electrical storage media such as RAM and ROM; and hybrids of these categories such as magnetic/optical storage media. A skilled artisan can readily appreciate how any of the presently known computer readable mediums can be used to create a manufacture comprising computer readable medium having recorded thereon a nucleotide sequence of the present invention. As used herein, "recorded" refers to a process for storing information on computer readable medium. A skilled artisan can readily adopt any of the presently known methods for recording information on computer readable medium to generate manufactures comprising the nucleotide sequence information of the present invention.

A variety of data storage structures are available to a skilled artisan for creating a computer readable medium having recorded thereon a nucleotide sequence of the present invention. The choice of the data storage structure will generally be based on the means chosen to access the stored information. In addition, a variety of data processor programs and formats can be used to store the nucleotide sequence information of the present invention on computer readable medium. The sequence information can be represented in a word processing text file, formatted in commercially-available software such as WordPerfect and Microsoft Word, or represented in the form of an ASCII file, stored in a database application, such as DB2, Sybase, Oracle, or the like. A skilled artisan can readily adapt any number of data processor structuring formats (*e.g.* text file or database) in order to obtain computer readable medium having recorded thereon the nucleotide sequence information of the present invention.

By providing any of the nucleotide sequences SEQ ID NO: 1-5497 or a representative fragment thereof; or a nucleotide sequence at least 95% identical to any of the nucleotide sequences of SEQ ID NO: 1-5497 in computer readable form, a skilled artisan can routinely access the sequence information for a variety of purposes. Computer software is publicly available which allows a skilled artisan to access sequence information provided in a computer readable medium. The examples which follow demonstrate how software which implements the BLAST (Altschul et al., J. Mol. Biol. 215:403-410 (1990)) and BLAZE (Brutlag et al., Comp. Chem. 17:203-207 (1993)) search algorithms on a Sybase system is used to identify open reading frames (ORFs) within a nucleic acid sequence. Such ORFs may be protein encoding fragments and may be useful in producing commercially important proteins such as enzymes used in fermentation reactions and in the production of commercially useful metabolites.

As used herein, "a computer-based system" refers to the hardware means, software means, and data storage means used to analyze the nucleotide sequence information of the present invention. The minimum hardware means of the computer-based systems of the present invention comprises a central processing unit (CPU), input means, output means, and data storage means. A skilled artisan can readily appreciate that any one of the currently available computer-based systems are suitable for use in the present invention. As stated above, the computer-based systems of the present invention comprise a data storage means having stored therein a nucleotide sequence of the present invention and the necessary hardware means and software means for supporting and implementing a search means. As used herein, "data storage means" refers to memory which can store nucleotide sequence information of the present invention, or a memory access means which can access manufactures having recorded thereon the nucleotide sequence information of the present invention.

As used herein, "search means" refers to one or more programs which are implemented on the computer-based system to compare a target sequence or target structural motif with the sequence information stored within the data storage means. Search means are used to identify fragments or regions of a known sequence which match a particular target sequence or target motif. A variety of known algorithms are disclosed publicly and a variety of commercially available software for conducting search means are and can be used in the computer-based systems of the present invention. Examples of such software includes, but is not limited to, Smith-Waterman, MacPattern (EMBL), BLASTN and BLASTA (NPOLYPEPTIDEIA). A skilled artisan can readily recognize that any one of the available algorithms or implementing software packages for conducting homology searches can be adapted for use in the present computer-based systems. As used herein, a "target sequence" can be any nucleic acid or amino acid sequence of six or more nucleotides or two or more amino acids. A skilled artisan can readily recognize that the longer a target sequence is, the less likely a target sequence will be present as a random occurrence in the database. The most preferred sequence length of a target sequence is from about 10 to 300 amino acids, more preferably from about 30 to 100 nucleotide residues. However, it is well recognized that searches for commercially important fragments, such as sequence fragments involved in gene expression and protein processing, may be of shorter length.

As used herein, "a target structural motif," or "target motif," refers to any rationally selected sequence or combination of sequences in which the sequence(s) are chosen based on a three-dimensional configuration which is formed upon the folding of the target motif. There are a variety of target motifs known in the art. Protein target motifs include, but are not limited to, enzyme active sites and signal sequences. Nucleic acid target motifs include, but are not limited

to, promoter sequences, hairpin structures and inducible expression elements (protein binding sequences).

#### 4.15 TRIPLE HELIX FORMATION

5 In addition, the fragments of the present invention, as broadly described, can be used to control gene expression through triple helix formation or antisense DNA or RNA, both of which methods are based on the binding of a polynucleotide sequence to DNA or RNA.

Polynucleotides suitable for use in these methods are preferably 20 to 40 bases in length and are designed to be complementary to a region of the gene involved in transcription (triple helix - see 10 Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 15241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Olmno, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA 15 transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide.

#### 4.16 DIAGNOSTIC ASSAYS AND KITS

20 The present invention further provides methods to identify the presence or expression of one of the ORFs of the present invention, or homolog thereof, in a test sample, using a nucleic acid probe or antibodies of the present invention, optionally conjugated or otherwise associated with a suitable label.

In general, methods for detecting a polynucleotide of the invention can comprise 25 contacting a sample with a compound that binds to and forms a complex with the polynucleotide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a polynucleotide of the invention is detected in the sample. Such methods can also comprise contacting a sample under stringent hybridization conditions with nucleic acid primers that anneal to a polynucleotide of the invention under such conditions, and amplifying annealed 30 polynucleotides, so that if a polynucleotide is amplified, a polynucleotide of the invention is detected in the sample.

In general, methods for detecting a polypeptide of the invention can comprise contacting a sample with a compound that binds to and forms a complex with the polypeptide for a period sufficient to form the complex, and detecting the complex, so that if a complex is detected, a 35 polypeptide of the invention is detected in the sample.

In detail, such methods comprise incubating a test sample with one or more of the antibodies or one or more of the nucleic acid probes of the present invention and assaying for binding of the nucleic acid probes or antibodies to components within the test sample.

Conditions for incubating a nucleic acid probe or antibody with a test sample vary.

5 Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid probe or antibody used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or immunological assay formats can readily be adapted to employ the nucleic acid probes or antibodies of the present invention. Examples of such assays can be found in Chard,  
10 T., An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G.R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985). The test samples of the  
15 present invention include cells, protein or membrane extracts of cells, or biological fluids such as sputum, blood, serum, plasma, or urine. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing protein extracts or membrane extracts of cells are well known in the art and can be readily be adapted in order to obtain a  
20 sample which is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention. Specifically, the invention provides a compartment kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the probes or antibodies of the present  
25 invention; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound probe or antibody.

In detail, a compartment kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers or strips of plastic or paper. Such containers allows one to efficiently transfer reagents from one compartment to  
30 another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the antibodies used in the assay, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which  
35 contain the reagents used to detect the bound antibody or probe. Types of detection reagents

include labeled nucleic acid probes, labeled secondary antibodies, or in the alternative, if the primary antibody is labeled, the enzymatic, or antibody binding reagents which are capable of reacting with the labeled antibody. One skilled in the art will readily recognize that the disclosed probes and antibodies of the present invention can be readily incorporated into one of the established kit formats which are well known in the art.

#### 4.17 MEDICAL IMAGING

The novel polypeptides and binding partners of the invention are useful in medical imaging of sites expressing the molecules of the invention (*e.g.*, where the polypeptide of the invention is involved in the immune response, for imaging sites of inflammation or infection). See, *e.g.*, Kunkel et al., U.S. Pat. NO. 5,413,778. Such methods involve chemical attachment of a labeling or imaging agent, administration of the labeled polypeptide to a subject in a pharmaceutically acceptable carrier, and imaging the labeled polypeptide *in vivo* at the target site.

#### 4.18 SCREENING ASSAYS

Using the isolated proteins and polynucleotides of the invention, the present invention further provides methods of obtaining and identifying agents which bind to a polypeptide encoded by an ORF corresponding to any of the nucleotide sequences set forth in SEQ ID NO: 1-5497, or bind to a specific domain of the polypeptide encoded by the nucleic acid. In detail, said method comprises the steps of:

- (a) contacting an agent with an isolated protein encoded by an ORF of the present invention, or nucleic acid of the invention; and
- (b) determining whether the agent binds to said protein or said nucleic acid.

In general, therefore, such methods for identifying compounds that bind to a polynucleotide of the invention can comprise contacting a compound with a polynucleotide of the invention for a time sufficient to form a polynucleotide/compound complex, and detecting the complex, so that if a polynucleotide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Likewise, in general, therefore, such methods for identifying compounds that bind to a polypeptide of the invention can comprise contacting a compound with a polypeptide of the invention for a time sufficient to form a polypeptide/compound complex, and detecting the complex, so that if a polypeptide/compound complex is detected, a compound that binds to a polynucleotide of the invention is identified.

Methods for identifying compounds that bind to a polypeptide of the invention can also comprise contacting a compound with a polypeptide of the invention in a cell for a time sufficient to form a polypeptide/compound complex, wherein the complex drives expression of a receptor gene sequence in the cell, and detecting the complex by detecting reporter gene sequence expression, so that if a polypeptide/compound complex is detected, a compound that binds a polypeptide of the invention is identified.

Compounds identified via such methods can include compounds which modulate the activity of a polypeptide of the invention (that is, increase or decrease its activity, relative to activity observed in the absence of the compound). Alternatively, compounds identified via such methods can include compounds which modulate the expression of a polynucleotide of the invention (that is, increase or decrease expression relative to expression levels observed in the absence of the compound). Compounds, such as compounds identified via the methods of the invention, can be tested using standard assays well known to those of skill in the art for their ability to modulate activity/expression.

The agents screened in the above assay can be, but are not limited to, peptides, carbohydrates, vitamin derivatives, or other pharmaceutical agents. The agents can be selected and screened at random or rationally selected or designed using protein modeling techniques.

For random screening, agents such as peptides, carbohydrates, pharmaceutical agents and the like are selected at random and are assayed for their ability to bind to the protein encoded by the ORF of the present invention. Alternatively, agents may be rationally selected or designed. As used herein, an agent is said to be "rationally selected or designed" when the agent is chosen based on the configuration of the particular protein. For example, one skilled in the art can readily adapt currently available procedures to generate peptides, pharmaceutical agents and the like, capable of binding to a specific peptide sequence, in order to generate rationally designed anti-peptide peptides, for example see Hurby et al., Application of Synthetic Peptides: Antisense Peptides," In Synthetic Peptides, A User's Guide, W.H. Freeman, NY (1992), pp. 289-307, and Kaspczak et al., Biochemistry 28:9230-8 (1989), or pharmaceutical agents, or the like.

In addition to the foregoing, one class of agents of the present invention, as broadly described, can be used to control gene expression through binding to one of the ORFs or EMFs of the present invention. As described above, such agents can be randomly screened or rationally designed/selected. Targeting the ORF or EMF allows a skilled artisan to design sequence specific or element specific agents, modulating the expression of either a single ORF or multiple ORFs which rely on the same EMF for expression control. One class of DNA binding agents are agents which contain base residues which hybridize or form a triple helix formation by binding to DNA or RNA. Such agents can be based on the classic phosphodiester,



ribonucleic acid backbone, or can be a variety of sulfhydryl or polymeric derivatives which have base attachment capacity.

Agents suitable for use in these methods preferably contain 20 to 40 bases and are designed to be complementary to a region of the gene involved in transcription (triple helix - see  
5 Lee et al., Nucl. Acids Res. 6:3073 (1979); Cooney et al., Science 241:456 (1988); and Dervan et al., Science 251:1360 (1991)) or to the mRNA itself (antisense - Okano, J. Neurochem. 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression, CRC Press, Boca Raton, FL (1988)). Triple helix-formation optimally results in a shut-off of RNA transcription from DNA, while antisense RNA hybridization blocks translation of an mRNA molecule into  
10 polypeptide. Both techniques have been demonstrated to be effective in model systems. Information contained in the sequences of the present invention is necessary for the design of an antisense or triple helix oligonucleotide and other DNA binding agents.

Agents that bind to a protein encoded by one of the ORFs of the present invention can be used as a diagnostic agent. Agents which bind to a protein encoded by one of the ORFs of the  
15 present invention can be formulated using known techniques to generate a pharmaceutical composition.

#### 4.19 USE OF NUCLEIC ACIDS AS PROBES

Another aspect of the subject invention is to provide for polypeptide-specific nucleic acid  
20 hybridization probes capable of hybridizing with naturally occurring nucleotide sequences. The hybridization probes of the subject invention may be derived from any of the nucleotide sequences SEQ ID NO: 1-5497. Because the corresponding gene is only expressed in a limited number of tissues, a hybridization probe derived from any of the nucleotide sequences SEQ ID NO: 1-5497 can be used as an indicator of the presence of RNA of cell type of such a tissue  
25 in a sample.

Any suitable hybridization technique can be employed, such as, for example, in situ hybridization. PCR as described in US Patents Nos. 4,683,195 and 4,965,188 provides additional uses for oligonucleotides based upon the nucleotide sequences. Such probes used in PCR may be of recombinant origin, may be chemically synthesized, or a mixture of both. The  
30 probe will comprise a discrete nucleotide sequence for the detection of identical sequences or a degenerate pool of possible sequences for identification of closely related genomic sequences.

Other means for producing specific hybridization probes for nucleic acids include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art and are commercially available and may be used to synthesize RNA probes  
35 *in vitro* by means of the addition of the appropriate RNA polymerase as T7 or SP6 RNA

polymerase and the appropriate radioactively labeled nucleotides. The nucleotide sequences may be used to construct hybridization probes for mapping their respective genomic sequences. The nucleotide sequence provided herein may be mapped to a chromosome or specific regions of a chromosome using well known genetic and/or chromosomal mapping techniques. These techniques include in situ hybridization, linkage analysis against known chromosomal markers, hybridization screening with libraries or flow-sorted chromosomal preparations specific to known chromosomes, and the like. The technique of fluorescent in situ hybridization of chromosome spreads has been described, among other places, in Verma et al (1988) Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York NY.

Fluorescent *in situ* hybridization of chromosomal preparations and other physical chromosome mapping techniques may be correlated with additional genetic map data. Examples of genetic map data can be found in the 1994 Genome Issue of Science (265:1981f). Correlation between the location of a nucleic acid on a physical chromosomal map and a specific disease (or predisposition to a specific disease) may help delimit the region of DNA associated with that genetic disease. The nucleotide sequences of the subject invention may be used to detect differences in gene sequences between normal, carrier or affected individuals.

#### 4.20 PREPARATION OF SUPPORT BOUND OLIGONUCLEOTIDES

Oligonucleotides, *i.e.*, small nucleic acid segments, may be readily prepared by, for example, directly synthesizing the oligonucleotide by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer.

Support bound oligonucleotides may be prepared by any of the methods known to those of skill in the art using any suitable support such as glass, polystyrene or Teflon. One strategy is to precisely spot oligonucleotides synthesized by standard synthesizers. Immobilization can be achieved using passive adsorption (Inouye & Hondo, (1990) J. Clin. Microbiol. 28(6) 1469-72); using UV light (Nagata *et al.*, 1985; Dahlen *et al.*, 1987; Morrissey & Collins, (1989) Mol. Cell Probes 3(2) 189-207) or by covalent binding of base modified DNA (Keller *et al.*, 1988; 1989); all references being specifically incorporated herein.

Another strategy that may be employed is the use of the strong biotin-streptavidin interaction as a linker. For example, Broude *et al.* (1994) Proc. Natl. Acad. Sci. USA 91(8) 3072-6, describe the use of biotinylated probes, although these are duplex probes, that are immobilized on streptavidin-coated magnetic beads. Streptavidin-coated beads may be purchased from Dynal, Oslo. Of course, this same linking chemistry is applicable to coating any surface with streptavidin. Biotinylated probes may be purchased from various sources, such as, *e.g.*, Operon Technologies (Alameda, CA).

Nunc Laboratories (Naperville, IL) is also selling suitable material that could be used. Nunc Laboratories have developed a method by which DNA can be covalently bound to the microwell surface termed CovaLink NH. CovaLink NH is a polystyrene surface grafted with secondary amino groups (>NH) that serve as bridge-heads for further covalent coupling. CovaLink Modules may be purchased from Nunc Laboratories. DNA molecules may be bound to CovaLink exclusively at the 5'-end by a phosphoramidate bond, allowing immobilization of more than 1 pmol of DNA (Rasmussen *et al.*, (1991) *Anal. Biochem.* 198(1) 138-42).

The use of CovaLink NH strips for covalent binding of DNA molecules at the 5'-end has been described (Rasmussen *et al.*, (1991). In this technology, a phosphoramidate bond is employed (Chu *et al.*, (1983) *Nucleic Acids Res.* 11(8) 6513-29). This is beneficial as immobilization using only a single covalent bond is preferred. The phosphoramidate bond joins the DNA to the CovaLink NH secondary amino groups that are positioned at the end of spacer arms covalently grafted onto the polystyrene surface through a 2 nm long spacer arm. To link an oligonucleotide to CovaLink NH via an phosphoramidate bond, the oligonucleotide terminus must have a 5'-end phosphate group. It is, perhaps, even possible for biotin to be covalently bound to CovaLink and then streptavidin used to bind the probes.

More specifically, the linkage method includes dissolving DNA in water (7.5 ng/ul) and denaturing for 10 min. at 95°C and cooling on ice for 10 min. Ice-cold 0.1 M 1-methylimidazole, pH 7.0 (1-MeIm<sub>7</sub>), is then added to a final concentration of 10 mM 1-MeIm<sub>7</sub>. A ss DNA solution is then dispensed into CovaLink NH strips (75 ul/well) standing on ice.

Carbodiimide 0.2 M 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (EDC), dissolved in 10 mM 1-MeIm<sub>7</sub>, is made fresh and 25 ul added per well. The strips are incubated for 5 hours at 50°C. After incubation the strips are washed using, *e.g.*, Nunc-Immuno Wash; first the wells are washed 3 times, then they are soaked with washing solution for 5 min., and finally they are washed 3 times (where in the washing solution is 0.4 N NaOH, 0.25% SDS heated to 50°C).

It is contemplated that a further suitable method for use with the present invention is that described in PCT Patent Application WO 90/03382 (Southern & Maskos), incorporated herein by reference. This method of preparing an oligonucleotide bound to a support involves attaching a nucleoside 3'-reagent through the phosphate group by a covalent phosphodiester link to aliphatic hydroxyl groups carried by the support. The oligonucleotide is then synthesized on the supported nucleoside and protecting groups removed from the synthetic oligonucleotide chain under standard conditions that do not cleave the oligonucleotide from the support. Suitable reagents include nucleoside phosphoramidite and nucleoside hydrogen phosphorate.

An on-chip strategy for the preparation of DNA probe for the preparation of DNA probe arrays may be employed. For example, addressable laser-activated photodeprotection may be

employed in the chemical synthesis of oligonucleotides directly on a glass surface, as described by Fodor *et al.* (1991) Science 251(4995) 767-73, incorporated herein by reference. Probes may also be immobilized on nylon supports as described by Van Ness *et al.* (1991) Nucleic Acids Res. 19(12) 3345-50; or linked to Teflon using the method of Duncan & Cavalier (1988) Anal. Biochem. 169(1) 104-8; all references being specifically incorporated herein.

To link an oligonucleotide to a nylon support, as described by Van Ness *et al.* (1991), requires activation of the nylon surface via alkylation and selective activation of the 5'-amine of oligonucleotides with cyanuric chloride.

One particular way to prepare support bound oligonucleotides is to utilize the light-generated synthesis described by Pease *et al.*, (1994) PNAS USA 91(11) 5022-6, incorporated herein by reference). These authors used current photolithographic techniques to generate arrays of immobilized oligonucleotide probes (DNA chips). These methods, in which light is used to direct the synthesis of oligonucleotide probes in high-density, miniaturized arrays, utilize photolabile 5'-protected *N*-acyl-deoxynucleoside phosphoramidites, surface linker chemistry and versatile combinatorial synthesis strategies. A matrix of 256 spatially defined oligonucleotide probes may be generated in this manner.

#### 4.21 PREPARATION OF NUCLEIC ACID FRAGMENTS

The nucleic acids may be obtained from any appropriate source, such as cDNAs, genomic DNA, chromosomal DNA, microdissected chromosome bands, cosmid or YAC inserts, and RNA, including mRNA without any amplification steps. For example, Sambrook *et al.* (1989) describes three protocols for the isolation of high molecular weight DNA from mammalian cells (p. 9.14-9.23).

DNA fragments may be prepared as clones in M13, plasmid or lambda vectors and/or prepared directly from genomic DNA or cDNA by PCR or other amplification methods. Samples may be prepared or dispensed in multiwell plates. About 100-1000 ng of DNA samples may be prepared in 2-500 ml of final volume.

The nucleic acids would then be fragmented by any of the methods known to those of skill in the art including, for example, using restriction enzymes as described at 9.24-9.28 of Sambrook *et al.* (1989), shearing by ultrasound and NaOH treatment.

Low pressure shearing is also appropriate, as described by Schriefer *et al.* (1990) Nucleic Acids Res. 18(24) 7455-6, incorporated herein by reference). In this method, DNA samples are passed through a small French pressure cell at a variety of low to intermediate pressures. A lever device allows controlled application of low to intermediate pressures to the cell. The results of

these studies indicate that low-pressure shearing is a useful alternative to sonic and enzymatic DNA fragmentation methods.

One particularly suitable way for fragmenting DNA is contemplated to be that using the two base recognition endonuclease, *CviJI*, described by Fitzgerald *et al.* (1992) Nucleic Acids Res.

20(14) 3753-62. These authors described an approach for the rapid fragmentation and fractionation of DNA into particular sizes that they contemplated to be suitable for shotgun cloning and sequencing.

The restriction endonuclease *CviJI* normally cleaves the recognition sequence PuGCPy between the G and C to leave blunt ends. Atypical reaction conditions, which alter the specificity of this enzyme (*CviJI*\*\*), yield a quasi-random distribution of DNA fragments from the small molecule pUC19 (2688 base pairs). Fitzgerald *et al.* (1992) quantitatively evaluated the randomness of this fragmentation strategy, using a *CviJI*\*\* digest of pUC19 that was size fractionated by a rapid gel filtration method and directly ligated, without end repair, to a lac Z minus M13 cloning vector. Sequence analysis of 76 clones showed that *CviJI*\*\* restricts pyGCPy and PuGCPu, in addition to PuGCPy sites, and that new sequence data is accumulated at a rate consistent with random fragmentation.

As reported in the literature, advantages of this approach compared to sonication and agarose gel fractionation include: smaller amounts of DNA are required (0.2-0.5 ug instead of 2-5 ug); and fewer steps are involved (no preligation, end repair, chemical extraction, or agarose gel electrophoresis and elution are needed).

Irrespective of the manner in which the nucleic acid fragments are obtained or prepared, it is important to denature the DNA to give single stranded pieces available for hybridization. This is achieved by incubating the DNA solution for 2-5 minutes at 80-90°C. The solution is then cooled quickly to 2°C to prevent renaturation of the DNA fragments before they are contacted with the chip. Phosphate groups must also be removed from genomic DNA by methods known in the art.

#### 4.22 PREPARATION OF DNA ARRAYS

Arrays may be prepared by spotting DNA samples on a support such as a nylon membrane. Spotting may be performed by using arrays of metal pins (the positions of which correspond to an array of wells in a microtiter plate) to repeated by transfer of about 20 nl of a DNA solution to a nylon membrane. By offset printing, a density of dots higher than the density of the wells is achieved. One to 25 dots may be accommodated in 1 mm<sup>2</sup>, depending on the type of label used. By avoiding spotting in some preselected number of rows and columns, separate subsets (subarrays) may be formed. Samples in one subarray may be the same genomic segment of DNA (or the same gene) from different individuals, or may be different, overlapped genomic clones. Each of the

subarrays may represent replica spotting of the same samples. In one example, a selected gene segment may be amplified from 64 patients. For each patient, the amplified gene segment may be in one 96-well plate (all 96 wells containing the same sample). A plate for each of the 64 patients is prepared. By using a 96-pin device, all samples may be spotted on one 8 x 12 cm membrane.

- 5 Subarrays may contain 64 samples, one from each patient. Where the 96 subarrays are identical, the dot span may be 1 mm<sup>2</sup> and there may be a 1 mm space between subarrays.

Another approach is to use membranes or plates (available from NUNC, Naperville, Illinois) which may be partitioned by physical spacers *e.g.* a plastic grid molded over the membrane, the grid being similar to the sort of membrane applied to the bottom of multiwell plates, or hydrophobic  
10 strips. A fixed physical spacer is not preferred for imaging by exposure to flat phosphor-storage screens or x-ray films.

The present invention is illustrated in the following examples. Upon consideration of the present disclosure, one of skill in the art will appreciate that many other embodiments and variations may be made in the scope of the present invention. Accordingly, it is intended that the broader  
15 aspects of the present invention not be limited to the disclosure of the following examples. The present invention is not to be limited in scope by the exemplified embodiments which are intended as illustrations of single aspects of the invention, and compositions and methods which are functionally equivalent are within the scope of the invention. Indeed, numerous modifications and variations in the practice of the invention are expected to occur to those skilled in the art upon  
20 consideration of the present preferred embodiments. Consequently, the only limitations which should be placed upon the scope of the invention are those which appear in the appended claims.

All references cited within the body of the instant specification are hereby incorporated by reference in their entirety.

## 5.0 EXAMPLES

### 25 5.1 EXAMPLE 1

#### Novel Nucleic Acid Sequences Obtained From Various Libraries

A plurality of novel nucleic acids were obtained from cDNA libraries prepared from various human tissues and in some cases isolated from a genomic library derived from human chromosome using standard PCR, SBH sequence signature analysis and Sanger sequencing techniques. The  
30 inserts of the library were amplified with PCR using primers specific for the vector sequences which flank the inserts. Clones from cDNA libraries were spotted on nylon membrane filters and screened with oligonucleotide probes (*e.g.*, 7-mers) to obtain signature sequences. The clones were clustered into groups of similar or identical sequences. Representative clones were selected for sequencing.

In some cases, the 5' sequence of the amplified inserts was then deduced using a typical Sanger sequencing protocol. PCR products were purified and subjected to fluorescent dye terminator cycle sequencing. Single pass gel sequencing was done using a 377 Applied Biosystems (ABI) sequencer to obtain the novel nucleic acid sequences. In some cases RACE (Rapid Amplification of cDNA Ends) was performed to further extend the sequence in the 5' direction.

## 5.2 EXAMPLE 2

### Novel Contigs

The novel contigs of the invention were assembled from sequences that were obtained from a cDNA library by methods described in Example 1 above, and in some cases sequences obtained from one or more public databases. The sequences for the resulting nucleic acid contigs are designated as SEQ ID NO: 1-5497 and are provided in the attached Sequence Listing. The contigs were assembled using an EST sequence as a seed. Then a recursive algorithm was used to extend the seed EST into an extended assemblage, by pulling additional sequences from different databases (*i.e.*, Hyseq's database containing EST sequences, dbEST version 115, gb pri 115, and UniGene version 103, and exons from public domain genomic sequences predicted by GenScan) that belong to this assemblage. The algorithm terminated when there was no additional sequences from the above databases that would extend the assemblage. Further, the inclusion of component sequences into the assemblage was based on a BLASTN hit to the extending assemblage with BLAST score greater than 300 and percent identity greater than 95%.

The novel predicted polypeptides (including proteins) encoded by the novel polynucleotides (SEQ ID NO: 1-5497) of the present invention are incorporated in the attached Sequence Listing. A subset of the predicted polypeptide sequences contain an unknown amino acid; a stop codon; a possible nucleotide deletion; or a possible nucleotide insertion. These sequences have also been shown in their entirety in Table 2. Table 2 also shows the corresponding start and stop nucleotide locations to each of SEQ ID NO: 1-5497. Table 2 also indicates the method by which the polypeptide was predicted. Method A refers to a polypeptide obtained by using a software program called FASTY (available from <http://fasta.bioch.virginia.edu>) which selects a polypeptide based on a comparison of the translated novel polynucleotide to known polynucleotides (W.R. Pearson, Methods in Enzymology, 183:63-98 (1990), herein incorporated by reference). Method B refers to a polypeptide obtained by using a software program called GenScan for human/vertebrate sequences (available from Stanford University, Office of Technology Licensing) that predicts the polypeptide based on a probabilistic model of gene structure/compositional properties (C. Burge and S. Karlin, J. Mol. Biol., 268:78-94 (1997), incorporated herein by reference). Method C refers

to a polypeptide obtained by using a Hyseq proprietary software program that translates the novel polynucleotide and its complementary strand into six possible amino acid sequences (forward and reverse frames) and chooses the polypeptide with the longest open reading frame.

The nearest neighbor results for SEQ ID NO: 1-5497 were obtained by a BLASTX  
5 version 2.0a1 19MP-WashU search against Genpept release 122 and Geneseq release 200105 (Derwent), using BLAST algorithm. The nearest neighbor result showed the closest homologue for SEQ ID NO: 1-5497. The nearest neighbor results for SEQ ID NO: 1-5497 are incorporated in the attached Sequence Listing.

Using eMatrix software package (Stanford University, Stanford, CA) (Wu et al., J.  
10 Comp. Biol., Vol. 6 pp. 219-235 (1999) herein incorporated by reference), all the sequences were examined to determine whether they had identifiable signature regions. The attached Sequence Listing provides the results obtained by eMatrix analysis for each polypeptide as follows: the signature region found in the indicated polypeptide sequences, the description of the signature, the eMatrix p-value(s) and the position(s) of the signature within the polypeptide sequence.

Using the pFam software program (Sonnhammer et al., Nucleic Acids Res., Vol. 26(1)  
15 pp. 320-322 (1998) herein incorporated by reference) all the polypeptide sequences were examined for domains with homology to certain peptide domains. The attached Sequence Listing provides the results obtained by pFam analysis for each polypeptide, namely: the name of the domain found, the description, the p-value and the pFam score for the identified domain  
20 within the sequence.

Tables 1 and 2 follow. Table 1 shows the various tissue sources of SEQ ID NO: 1-5497. Table 2 shows the start and stop nucleotides for the translated amino acid sequence for which each assemblage encodes. Table 2 also provides a correlation between the amino acid sequences set forth in the Sequence Listing, the nucleotide sequences set forth in the Sequence Listing and the SEQ ID  
25 NO: in USSN 09/770,160.



Table 1

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
adult brain	GIBCO	AB3001	81-82 126 136 154-156 175-177 213-215 278-283 346-349 445-446 459 491-492 543 561-562 652-653 709-711 755-757 794-795 822-823 899 924 971-988 995 997-998 1017- 1021 1026-1027 1036-1037 1048 1085 1128 1143 1154 1173 1202-1204 1269-1270 1290- 1291 1300-1301 1320-1321 1353-1355 1357- 1359 1363-1371 1388 1394-1396 1410 1415- 1417 1422-1424 1426 1455-1456 1465-1470 1508-1510 1533-1535 1541-1546 1550 1580- 1581 1585 1588-1589 1592 1603-1608 1648 1655 1663 1674-1682 1685 1709 1719-1721 1723 1727-1734 1746 1753 1755-1756 1773- 1774 1805-1806 1827-1829 1839-1847 1876- 1877 1915-1918 1951 2005 2021-2024 2027- 2034 2042-2043 2054 2057 2072-2074 2092 2096-2097 2118 2144-2145 2177 2188-2190 2193-2195 2208-2210 2214-2215 2251-2252 2281-2283 2288-2291 2294-2299 2331 2344 2382 2417-2420 2422 2430 2437 2439-2441 2446 2456 2483 2496 2499 2510-2513 2552 2656 2686 2741-2743 2746-2747 2774-2778 2783 2786 2842-2843 2857-2860 2865 2873- 2874 2879-2881 2883-2884 2960-2962 2976- 2977 3009 3136-3137 3139-3148 3167-3168 3170-3171 3174 3198 3207 3213-3214 3220- 3222 3230 3240 3257-3259 3276-3277 3280- 3282 3289-3290 3304-3307 3323-3324 3345- 3346 3394-3395 3456 3477-3478 3536-3543 3558-3562 3587 3689 3694-3696 3729-3730 3737-3738 3772 3822-3825 3831-3833 3864- 3865 3891 3963-3965 4001 4055-4056 4060- 4061 4093 4098 4112-4113 4123 4125 4136- 4141 4230-4231 4273-4274 4291-4295 4520 4546-4548 4569-4571 4575-4576 4691-4692 4740-4741 4796-4797 4804-4805 4864-4865 4900 4907-4909 5148-5149 5276-5277 5295- 5296 5298-5302 5464-5466
adult brain	GIBCO	ABD003	1-11 52 64 81-82 123 154-156 175-177 233 248 258-260 278-283 313-315 335 339 354 357-361 365 379-380 388-390 394 459 491- 492 557 561-562 574-577 582 597-598 607 652-653 670-671 677-678 682-684 719-722 743-744 794-795 799-800 814-816 818 822- 823 840-844 863-869 873-875 878 882-886 889-897 909-914 916-920 924 927 930-936 944-960 964-966 969 971-988 993-995 997- 999 1008-1009 1017-1021 1023-1027 1036-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			1037 1042-1048 1050-1051 1053-1054 1063- 1068 1070-1071 1075 1089-1091 1110-1113 1117-1121 1128-1136 1143 1154 1156 1159- 1164 1172 1175 1180-1184 1198-1204 1217- 1218 1235-1236 1244-1246 1249-1255 1269- 1273 1281-1282 1297 1300-1301 1307 1315- 1316 1319-1322 1349-1350 1352-1355 1357- 1358 1374 1388-1393 1398-1399 1410 1413 1422-1424 1426 1438-1441 1446-1449 1451- 1456 1463-1466 1473 1478-1479 1485 1498- 1499 1507-1510 1516-1517 1532 1536-1539 1541-1546 1551-1552 1559-1560 1580-1581 1588-1589 1605-1608 1612 1620-1623 1639 1648 1654 1661-1663 1665 1671-1673 1685 1688-1690 1694-1699 1703-1704 1708-1709 1715-1716 1719-1721 1723 1727 1737-1739 1743-1746 1753-1756 1765-1769 1780-1783 1805-1817 1831-1838 1845-1851 1860 1870- 1875 1878 1900-1911 1915-1922 1926-1927 1951-1962 1964-1965 1978-1979 1981-1983 1990-1991 2000-2002 2005 2010-2013 2027- 2030 2038 2042-2043 2048 2050-2051 2057- 2061 2066-2067 2072-2074 2083-2084 2086- 2087 2092-2093 2096-2102 2107 2115-2116 2118 2125-2130 2144 2146-2147 2177 2186- 2188 2214-2215 2223 2230-2232 2251-2252 2254 2258-2260 2267-2270 2273 2281-2282 2284 2288-2291 2296-2299 2310 2318-2320 2324 2331 2333-2334 2377-2382 2389-2390 2403-2404 2416-2417 2419-2424 2430 2439- 2441 2444 2446-2447 2467 2469 2475 2483 2488 2499 2510-2513 2536-2538 2573-2575 2592 2594-2595 2597 2603-2604 2628-2632 2644-2648 2656 2666 2668 2672-2674 2677- 2680 2686 2696-2697 2726 2734 2745-2748 2751 2760 2763-2764 2768-2771 2777-2778 2780-2783 2786 2805-2806 2814 2820 2824- 2826 2828 2836-2839 2843 2854 2857-2860 2865 2894-2897 2906 2914-2917 2925-2929 2954 2960 2964 2969-2973 2996-2998 3009 3035-3036 3054 3084-3085 3088-3089 3094- 3095 3100 3110 3133-3135 3139-3148 3151- 3152 3158 3167-3168 3170-3173 3189-3191 3195 3199 3203-3204 3213-3214 3219 3223 3226-3228 3230-3233 3253-3255 3257-3259 3276-3277 3280-3282 3288-3290 3310-3311 3313 3323-3324 3331-3332 3339-3340 3345- 3346 3372-3373 3409-3417 3442 3477-3478 3491-3495 3505-3506 3536-3543 3554-3556 3558-3560 3576 3587-3589 3599-3601 3628-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult brain	Clontech	ABR001	3-11 70 137 175-177 478 491-492 597-598 755-757 796 852-854 910-914 964-966 1026-1027 1049 1158-1159 1173 1198-1201 1271 1274 1281-1282 1297 1351 1363-1371 1389 1479 1671-1673 1685 1719-1721 1784-1790 1870-1875 1900-1902 1919-1922 1926-1927 2035 2072-2074 2224-2228 2298-2299 2305-2306 2404 2419-2420 2436 2528-2531 2644 2713-2714 2751 2762 2774-2776 2786 2978 3113 3151-3152 3181-3183 3213-3214 3424-3427 3554-3556 3577-3582 3587 3595-3596 3638-3640 3663 3742-3744 3853 3911-3919 3931 3941-3942 3962 4036-4039 4077-4079 4125 4220-4223 4320 4545 4549 4570-4571 4672-4674 4738-4739 4764-4766 4781 4815 4910 5001-5003 5435-5437 5464-5466
adult brain	Clontech	ABR006	47 126 130 154-156 278-283 395 561-562 583-590 661-662 709-711 855-856 889-897 903-905 909 945 961-962 1063-1067 1069 1088 1095 1154-1155 1235-1236 1281-1282 1349-1350 1360-1362 1394 1418-1420 1580-1584 1626 1634-1637 1671-1673 1688-1689 1694-1698 1715-1716 1728-1734 1763-1764 1770-1771 1773-1774 1839-1844 1903-1911 1913-1914 2027-2030 2035 2054-2056 2076-2077 2121-2124 2145 2163-2168 2188 2197-2199 2214-2215 2445 2591-2592 2598 2650 2686 2737-2738 2745 2774-2778 2857-2860 3323-3324 3328-3330 3342-3344 3354 3396-3398 3498-3501 3536-3543 3658-3660 3856-3857 4300-4308 4379-4380 4410-4412 4451-4452 4481-4489 4549 4624-4626 4660 4824-4826 4832-4834 4967-4970 5050-5052 5278-5279
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult brain	Clontech	ABR011	154-156 388-390 1076 1128 1182-1184 1193 1202-1204 1422-1424 2072-2074 2144 2251- 2252 2549-2550 4062-4064 5298-5302
adult brain	BioChain	ABR012	440-441 602-603 889-897 997-998 1582- 1584 1719-1721 1780-1783 2072-2074 2186- 2187 2223 2377-2379 3394-3395 4291-4295 4581-4582 5123-5124
adult brain	Invitrogen	ABR013	341-344 491-492 1205-1207 1580-1581 1599-1602 1857-1859 1925 2072-2074 2186- 2187 2208-2210 2377-2379 2469 3250-3252 3304-3307 4267-4270 4796-4797
adult brain	Invitrogen	ABT004	12-13 38 52 70 92-95 126 175-177 255-257 291 341-344 346-349 354 478 557 583-590 612-620 675 789-793 796 840-844 871-872 879-884 909 919-920 964-966 997-998 1017- 1021 1026-1027 1042-1043 1051 1070-1071 1076 1088 1108 1151-1153 1160-1164 1193 1217-1218 1228-1229 1269-1270 1281-1282 1320-1321 1349-1350 1385 1427-1431 1467- 1469 1485 1532 1575-1576 1626 1629-1632 1640-1645 1708 1715-1716 1727 1742-1746 1773-1774 1799-1804 1807-1813 1852 1860 1865-1875 1900-1911 1948-1949 1954-1962 1964-1965 1981-1983 1990-1991 2010-2013 2036-2037 2054 2072-2074 2078-2082 2086- 2087 2143-2147 2174-2176 2186-2187 2224- 2228 2231-2232 2255-2257 2264 2284 2310- 2312 2369-2375 2397-2399 2419-2420 2436 2526-2527 2592 2604 2624 2626 2629-2631 2696-2697 2734 2751 2785 2813 2857-2860

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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cultured preadipocytes	Stratagene	ADP001	74-77 134 154-156 175-177 201-205 213-215 278-283 313-315 489-492 520-521 652-653 670-671 680-684 736-740 743-744 784-786 796 814-816 822-823 857-859 885-886 944 950 964-966 994 1028 1042-1043 1052 1069- 1071 1089-1091 1129-1130 1143 1154 1156 1172 1198-1204 1249-1255 1278-1280 1317- 1318 1320-1321 1351 1359 1380 1410 1455- 1456 1473 1507 1532-1535 1547-1548 1553- 1556 1559-1560 1588-1589 1611 1617-1619 1640-1645 1648 1663 1666 1723-1724 1727 1746 1755-1756 1765-1769 1773-1774 1780- 1783 1839-1844 1870-1877 1925 1990-1991 2060-2061 2118 2193-2195 2197-2199 2223 2234-2242 2298-2299 2310 2331 2380-2381 2443 2452-2454 2524-2525 2572-2573 2591- 2592 2594-2595 2604 2672-2674 2709-2711 2734 2739 2819 2843-2847 2861-2862 2899- 2900 2913 2925-2929 2979 2985 3013-3014 3159-3162 3181-3183 3189-3191 3220-3222 3253-3255 3285 3310-3311 3462 3486-3487 3587 3638-3640 3673-3677 3754 3804-3806 3815-3816 3871-3872 3969-3971 4014-4015 4036-4039 4068-4069 4140-4141 4241-4242 4254 4341 4534 4554-4555 4570-4571 4581- 4582 4622-4623 4740-4741 4864-4865 4910 5001-5003 5038-5039 5095-5097 5137-5140
adrenal gland	Clontech	ADR002	1-2 12-13 35 52 62 100-106 121-122 140-142 153-156 191-192 213-215 221 232 301-303 306 313-315 341-344 366-367 394 459 491- 492 513 551-553 583-590 592-595 652-653 670-671 719-722 728-733 743-744 747-750 755-757 772 784-786 814-816 847 849-851 889-897 909-914 916-920 944 946-949 961- 962 993-995 997-999 1049 1070-1071 1078 1089-1091 1117-1119 1128 1151-1153 1160- 1164 1175 1182-1184 1193 1220-1221 1269- 1270 1272-1273 1287 1307 1352 1355 1357- 1359 1407 1415-1417 1422-1423 1480 1485 1498-1499 1505 1507-1510 1526 1541-1546

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult heart	GIBCO	AHR001	45-46 52 56 100-106 133-134 140-142 154- 156 173 175-177 192 195-196 201-205 212- 218 227-230 235 278-283 286-287 301-303 313-315 323 332-333 341-344 346-352 366- 367 379-380 395 400-404 413-414 436 469 478 491-492 511 520-521 531-532 551-553 557 574-577 583-590 599-601 604 607 612- 620 652-653 675 677-678 680-685 697 707 743-744 784-786 789-796 799-800 814-816 822-823 847 885-886 889-897 915-920 924- 929 931-936 944-945 950 957-960 964-966 969 971-979 992 994-1002 1017-1027 1044- 1050 1052-1054 1056-1057 1063-1067 1070- 1071 1075 1110-1113 1117-1119 1127-1136 1139-1143 1154 1156 1159 1172-1173 1182- 1185 1192-1193 1202-1207 1220-1221 1228

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult kidney	GIBCO	AKD001	32-34 36-37 39-40 42 45-47 74-78 87 100- 106 116-119 136 165 175-177 213-218 220 223-231 235 244 252-253 258-260 278-283 298-300 313-320 324-325 332-333 341-344 346-349 364 366-367 379-380 394 396-398 419 436 440-441 445-446 452 474 491-492 498 519 548-553 557 574-577 583-590 602- 603 607 629-630 652-653 677-678 682-684 707 709-711 719-722 728-733 736-740 778- 786 789-793 799-800 806-808 814-816 822- 823 836-838 840-844 852-854 857-859 871- 875 879-886 889-897 899-905 909-915 919- 920 924-926 931-936 944-962 964-966 969- 974 980-988 994-995 997-998 1000-1009 1017-1021 1026-1027 1036-1040 1042-1043 1049-1050 1052 1063-1071 1075-1076 1078- 1079 1081-1082 1085 1088-1091 1110-1113 1116-1121 1127-1130 1137-1142 1151-1155 1159 1172-1173 1182-1184 1189-1193 1198- 1207 1217-1218 1220-1221 1230-1232 1235- 1236 1249-1260 1269-1271 1278-1280 1287 1294-1297 1300-1301 1307 1315-1321 1328 1334-1335 1349-1350 1352-1354 1357-1362 1374 1385-1389 1397-1399 1403-1407 1410 1414-1420 1422-1423 1425-1426 1435-1436 1438 1440-1441 1444 1451-1462 1465-1466 1470-1472 1475-1477 1479 1481-1485 1488- 1489 1498-1499 1504-1505 1507-1510 1515- 1517 1524 1527-1532 1536-1538 1540-1548 1551-1557 1561-1563 1569-1576 1579-1589 1591 1597 1603-1608 1611-1619 1625-1626 1634-1648 1653-1654 1656 1663-1665 1667- 1682 1685 1688-1692 1694-1698 1701-1704 1707-1708 1710-1716 1719-1721 1723-1724 1727-1739 1743-1746 1753 1755-1758 1763- 1771 1773-1783 1796-1798 1805-1806 1814- 1817 1830-1847 1857-1860 1865-1877 1882- 1885 1903-1911 1913-1922 1925-1927 1948- 1953 1964-1974 1978-1979 1981-1983 1993-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			1998 2004-2005 2010-2013 2021-2038 2042- 2043 2045-2047 2055-2061 2068-2083 2086- 2087 2092 2094 2096-2100 2111-2114 2116 2118 2125-2133 2137-2142 2144 2146-2147 2151-2152 2156-2160 2173-2181 2186-2188 2191-2195 2197-2199 2202-2203 2208-2213 2216-2221 2223-2230 2234-2242 2244-2248 2251-2252 2254-2257 2261 2267-2270 2272- 2273 2280-2282 2284 2288-2291 2296-2297 2302 2310 2318-2320 2331 2333-2334 2338- 2340 2368 2377-2382 2386 2388-2392 2403 2405-2415 2422-2424 2427 2430 2440-2441 2446-2447 2451 2467-2472 2475 2483-2485 2488 2490-2491 2496 2499 2510-2513 2521- 2525 2528-2531 2536 2546 2554-2556 2564- 2572 2574-2575 2579-2584 2591-2592 2596 2604 2629-2637 2645-2649 2672-2676 2693 2696-2697 2702-2706 2709-2711 2716-2718 2721 2726 2730 2734 2747-2748 2754-2758 2760-2761 2763 2768-2772 2774-2778 2781 2785 2800-2801 2805-2806 2809 2814 2818 2828 2836-2839 2842-2843 2854-2863 2865 2873-2874 2888 2894-2898 2901-2903 2913 2925-2929 2931-2939 2945-2946 2960-2962 2969-2976 2979 3009 3013-3014 3017-3022 3026-3027 3054 3076-3078 3082 3098-3100 3102-3105 3109 3136-3137 3139-3147 3151- 3162 3167-3168 3170-3174 3189-3191 3195 3204 3215-3216 3218 3224-3230 3234 3240 3242 3256-3267 3276-3277 3280-3282 3285 3288-3290 3292-3293 3296-3299 3313 3323- 3324 3331-3335 3339-3340 3342-3344 3367- 3368 3374-3382 3394-3398 3403-3404 3406- 3407 3409-3410 3428-3429 3438-3441 3443- 3445 3456 3462 3466-3468 3470-3471 3519 3535-3543 3554-3556 3561-3562 3576-3580 3589 3605 3610-3613 3619-3625 3628 3632- 3634 3638-3640 3664-3665 3667 3670-3671 3673-3677 3684 3686-3691 3716 3724-3725 3742-3744 3747 3760-3761 3780-3781 3815- 3816 3822-3824 3826 3830 3837-3838 3870 3880 3882-3883 3895 3897-3905 3911-3919 3939-3951 3955-3957 3959-3960 3966-3971 3997-3998 4014-4015 4036-4039 4055-4056 4060-4064 4071-4075 4077-4079 4082-4084 4093 4098 4101-4102 4114-4116 4119-4123 4136 4138-4143 4220-4223 4230-4235 4243- 4244 4252-4253 4255-4257 4260 4267-4270 4285-4288 4322 4335-4337 4342 4363 4383- 4384 4391-4393 4400 4430-4432 4439 4451-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult kidney	Invitrogen	AKT002	1-2 70 278-283 313-315 379-380 457 491- 492 574-577 582 604 652-653 699-701 707 709-711 719-722 764-771 794-795 814-816 822-823 840-844 906-909 924 944 950 963 975-988 993 995 1017-1021 1042-1043 1063- 1067 1070-1071 1076 1079 1110-1113 1117- 1119 1128 1137-1143 1172 1182-1184 1193 1208-1212 1220-1221 1235-1242 1278-1280 1287 1297 1315-1318 1323-1328 1355 1357- 1358 1360-1371 1374 1397 1405-1406 1414 1418-1420 1425 1457-1462 1488 1507 1515 1536-1538 1547-1548 1551-1552 1559-1560 1579 1626 1656 1664 1674-1682 1685-1689 1691-1693 1706 1708 1710-1716 1719-1721 1728-1734 1737-1739 1753 1773-1774 1845- 1851 1870-1875 1897 1903-1911 1913-1914 1925 1948-1949 1951-1953 1978-1979 1981- 1983 1990-1991 2004-2005 2017-2020 2027- 2030 2038 2048 2054 2062-2064 2072-2074 2076-2077 2116 2118 2125-2133 2156-2160 2174-2176 2179-2181 2186-2188 2208-2210 2214-2215 2224-2228 2275 2277 2296-2297 2321 2377-2379 2391 2397-2399 2421 2428 2452-2454 2473-2474 2492-2494 2499 2528- 2531 2536 2560 2579-2584 2592 2594-2595 2608-2616 2706 2734 2781 2785 2818 2843- 2845 2854 2861-2862 2886-2887 2974-2975 2979 2984 2996-2998 3008 3100 3139-3147 3149 3151-3152 3156-3157 3184 3195 3218 3250-3252 3260-3267 3269 3313 3325-3327 3336-3338 3341-3344 3424-3427 3550-3552 3554-3556 3590 3624-3625 3628 3658-3660 3663 3693 3791 3822-3824 3943-3948 4004 4040-4042 4055-4056 4076 4093 4109-4111 4232-4235 4241-4242 4275-4277 4534 4549 4622-4623 4633-4634 4740-4741 4764-4766

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult lung	GIBCO	ALG001	78 136 138-139 175-177 313-315 324-325 341-344 413-414 440-441 456 491-492 511 557 652-653 677-678 728-733 784-786 794-795 822-823 849-851 855-856 885-886 919-920 954-960 975-988 992-993 997-999 1003-1006 1017-1021 1026-1027 1042-1043 1053-1054 1075 1088 1129-1130 1143 1182-1184 1189-1191 1198-1201 1208-1212 1271 1297 1300-1301 1317-1318 1352-1355 1374 1407 1422-1423 1455-1462 1481-1484 1488-1489 1497 1507-1512 1516-1517 1532-1535 1541-1548 1551-1556 1582-1584 1588-1589 1591 1603-1604 1611 1617-1619 1663 1723 1727-1734 1742-1746 1753 1780-1783 1814-1817 1831-1834 1852 1870-1875 1919-1922 1925 1951 2005-2007 2038 2058-2061 2072-2074 2086-2087 2116 2118 2121-2136 2144 2153-2155 2163-2168 2179-2181 2186-2187 2214-2215 2223-2228 2230 2234-2242 2277 2283 2296-2299 2331 2380-2382 2389-2390 2467-2469 2473-2474 2499 2536 2553 2564-2571 2574-2575 2604 2672-2674 2677-2680 2749-2750 2759 2761 2774-2776 2843 2855-2856 2913 2957 2960 2969-2973 3081 3084-3085 3098-3099 3156-3157 3167-3168 3213-3214 3220-3222 3226-3228 3238 3256 3280-3282 3289-3290 3319-3322 3333-3335 3409-3410 3442 3466-3468 3558-3560 3588 3621-3625 3628 3689 3776-3777 3815-3816 3893 3908 4040-4042 4068-4069 4114-4116 4136 4232-4235 4291-4295 4335-4337 4404-4407 4439 4545 4672-4674 4756-4757 4796-4797 4804-4805 4886 4907-4909 5001-5003 5046-5047 5095-5097 5142-5143 5387-5388 5464-5466
lymph node	Clontech	ALN001	39-40 143-148 154-156 269 278-283 313-315 445-446 728-733 736-742 764-771 814-816 822-823 931-936 950 961-962 994 1000-1002 1017-1021 1129-1130 1139-1142 1151-1153 1182-1184 1198-1204 1244-1246 1256 1319 1359 1398-1399 1425 1438 1455-1462 1478 1504 1507 1511-1512 1532 1539 1547-1549 1553-1556 1575-1576 1617-1619 1648 1659-1660 1663 1719-1721 1735-1736 1753 1755-1756 1839-1844 1857-1859 1919-1922 1925 1951 1993-1998 2004 2038 2042-2043 2048

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			2060-2061 2086-2087 2107 2111-2114 2118 2125-2130 2137 2144-2145 2191-2195 2208- 2210 2214-2215 2223 2254 2277 2288-2291 2296-2297 2394 2470-2472 2483 2526-2527 2554-2556 2649 2774-2776 2852-2854 2861- 2862 2865 2888 2896-2897 2965-2968 3029 3133-3135 3189-3191 3242 3250-3252 3280- 3282 3289-3290 3312 3333-3335 3411-3417 3577-3580 3638-3640 3716 3817-3821 3878- 3879 3962 4023 4090-4092 4134 4140-4141 4219 4285-4286 4581-4582 4796-4797 4864- 4865 4907-4909 5001-5003 5261-5267 5272- 5274 5323-5325 5332-5333 5335-5343 5423- 5425 5444
young liver	GIBCO	ALV001	48-50 78 100-110 210-211 255-257 261-266 278-283 286-287 313-320 332-333 381-383 395 419 435-436 491-492 548-553 574-577 652-653 677-678 709-711 755-757 784-786 789-793 799-803 806-808 822-823 840-844 852-854 910-914 916-918 924 944 969 995 997-998 1056-1057 1063-1068 1085 1089- 1091 1116 1120-1121 1128-1130 1139-1142 1151-1155 1172 1177-1179 1182-1184 1189- 1191 1198-1201 1205-1207 1217-1218 1220- 1221 1230-1232 1249-1256 1269-1273 1290- 1291 1300-1301 1310-1314 1323-1328 1357- 1358 1360-1362 1374 1410 1418-1420 1479- 1484 1497 1507 1516-1517 1527-1531 1541- 1546 1551-1552 1557 1579-1581 1585 1590 1592 1613-1619 1626 1656 1664 1685 1691- 1692 1694-1698 1701-1702 1708-1709 1723 1725-1726 1735-1739 1753 1759-1762 1765- 1771 1773-1774 1780-1790 1796-1798 1827- 1829 1835-1838 1848-1852 1865-1875 1882- 1885 1903-1911 1913-1914 1919-1922 1925 1951 1964-1965 1978-1979 2005 2031-2034 2060-2061 2075 2086-2091 2096-2097 2118 2144 2153-2160 2174-2176 2188 2200-2201 2223-2228 2234-2242 2244-2245 2281-2282 2288-2291 2321 2358 2380-2382 2414-2415 2423-2424 2427 2447 2451 2469 2477-2479 2484-2485 2503-2504 2510 2533 2543-2544 2560 2564-2571 2579-2584 2587 2648 2761 2836-2839 2843 2865 2873-2874 2879-2881 2945-2946 2951-2952 2957 2974-2975 3013- 3014 3076-3078 3139-3147 3151-3152 3156- 3157 3181-3183 3195 3226-3228 3242 3250- 3252 3280-3282 3299 3310-3311 3328-3330 3345-3346 3403-3404 3456 3462 3561-3562 3599-3601 3619-3625 3628 3654-3657 3815-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			3816 3828 3969-3971 4023 4062-4064 4090-4092 4121-4122 4228 4373-4375 4403 4451-4452 4563 4622-4623 4635-4637 4738-4739 4768-4771 4796-4797 4815 4899 4907-4909 4915-4916 4998-4999 5001-5003 5045 5075-5077 5082-5083 5130-5131 5166-5167 5226 5335-5343 5399-5403 5414-5415 5452-5453 5456-5457 5464-5466
adult liver	Invitrogen	ALV002	35-37 62 70 107-110 131-132 175-177 192 233 255-257 261-266 278-283 313-315 337 354 365 374-375 445-446 450-451 478 491-492 652-653 801-803 840-844 848 852-854 903-905 944 954-956 995 997-998 1003-1006 1026-1027 1032-1034 1042-1047 1049 1056-1060 1063-1071 1078 1089-1091 1117-1119 1139-1143 1151-1154 1158-1159 1177-1181 1188-1191 1193 1205-1207 1217-1218 1230-1232 1278-1282 1307 1310-1314 1323-1327 1337-1345 1351 1360-1371 1380 1451-1454 1485 1533-1535 1547-1548 1569-1574 1592 1626 1640-1647 1656 1663 1691-1692 1708-1709 1723 1725-1726 1735-1739 1759-1762 1770-1771 1773-1774 1827-1829 1835-1844 1913-1914 1919-1922 1925 1948-1949 1954-1962 1981-1983 2010-2013 2025-2026 2054 2060-2061 2118 2171 2174-2176 2186-2190 2193-2195 2208-2210 2223 2254 2267-2270 2276-2277 2296-2297 2308 2322 2338-2340 2380-2381 2499 2533 2536 2543-2544 2560 2579-2584 2629-2631 2648 2659-2662 2665 2741-2743 2800-2801 2828 2843 2865 2879-2882 2905 2914-2917 2925-2929 2957 2960-2962 2974-2975 3013-3014 3054 3089 3156-3157 3181-3183 3199 3220-3222 3229 3310-3311 3328-3330 3371-3373 3462 3466-3469 3472-3473 3536-3543 3577-3580 3667 3749-3752 3793 3997-3998 4014-4015 4036-4039 4082-4084 4096-4097 4282 4330-4331 4376-4377 4381 4451-4452 4616-4621 4633-4634 4636-4637 4649 4687-4689 4738-4739 4754-4755 4768-4771 4796-4797 5050-5052 5057-5065 5082-5083 5130-5131 5145 5148-5149 5164-5167 5229-5231 5335-5343 5367-5368 5387-5391 5414-5415 5451-5453
adult liver	Clontech	ALV003	341-344 370-371 849-851 946-949 1177-1179 1202-1204 1626 1759-1762 1770-1771 1913-1914 2484-2485 3328-3330 4403 4998-4999 5130-5131
adult ovary	Invitrogen	AOV001	12-13 32-34 39-40 42 44 47-50 52 63-64 70 74-78 87 100-110 116-119 133 135-139 153

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			173 175-177 185 201-205 212-215 220 222 227-230 233 245 267-268 277-283 286-287 291 301-303 313-315 321 341-344 357-361 364 372 376-377 379-380 394 396-398 436 445-446 459 462 474 478 491-495 509 511 520-524 538 543 545 551-553 561-562 574- 577 583-594 604-607 611-620 629-630 641 652-653 677-678 682-684 697 699-703 707- 711 719-722 728-733 743-744 747-750 755- 757 764-771 784-786 789-795 801-803 806- 808 814-816 822-825 836-837 840-844 855- 856 863-869 871-875 879-886 889-897 899- 908 910-914 916-920 924 927 930-936 944 950-962 964-966 969 971-988 990-995 997- 1006 1008-1009 1017-1027 1032-1040 1042- 1047 1049 1052-1054 1068 1070-1071 1075- 1076 1078-1079 1081-1082 1089-1091 1095 1108 1117-1121 1128-1142 1151-1156 1158- 1164 1171-1173 1175 1180-1185 1189-1193 1198-1207 1217-1218 1220-1221 1228-1232 1235-1242 1244-1246 1249-1256 1269-1271 1278-1280 1287 1290-1293 1297-1301 1307 1315-1328 1332-1335 1348-1359 1363-1371 1374 1380 1383-1384 1386-1389 1395-1396 1398-1399 1403-1410 1413-1417 1421-1423 1426 1432 1435-1436 1438-1444 1446-1449 1451-1464 1467-1473 1475-1480 1485 1488 1491-1494 1498-1499 1504-1505 1507-1512 1515-1517 1520 1527-1538 1541-1548 1550- 1557 1569-1576 1580-1589 1591 1603-1608 1611-1612 1617-1619 1621-1623 1625 1629- 1632 1638-1645 1648-1654 1656-1658 1663- 1664 1666-1670 1674-1682 1685-1686 1688- 1692 1694-1698 1701-1702 1707-1709 1717 1719-1721 1723 1727-1739 1743-1746 1753 1755-1756 1758 1763-1769 1780-1783 1792- 1817 1827-1830 1835-1838 1848-1853 1860 1865-1877 1879-1885 1900-1911 1915-1922 1925-1936 1948-1953 1964-1965 1978-1979 1981-1983 1990-1991 1993-1998 2000-2002 2004-2005 2017-2024 2027-2037 2042-2043 2045-2048 2052-2061 2066-2067 2076-2077 2080-2082 2086-2091 2093-2094 2096-2100 2111-2115 2118 2125-2133 2138-2147 2151- 2160 2174-2177 2179-2181 2186-2187 2189- 2195 2197-2201 2204-2215 2223 2229 2231- 2232 2234-2242 2251-2252 2254-2262 2264- 2265 2267-2271 2273 2275 2277 2281-2284 2286-2291 2296-2300 2321 2331 2380-2381 2386-2392 2395 2397-2399 2403 2414-2415

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			4674 4681-4683 4691-4692 4740-4741 4748-4749 4751-4753 4764-4766 4777-4780 4784-4786 4796-4797 4804-4805 4812 4820 4854 4861-4865 4874-4875 4886 4902 4907-4910 4912 4918-4920 4923-4925 4953 4956-4957 4976-4979 5001-5003 5025 5040 5050-5052 5057-5065 5085-5088 5095-5097 5109 5115 5123-5127 5148-5149 5154-5157 5173 5222-5224 5241-5242 5251 5259 5261-5267 5276-5277 5281 5284-5289 5308-5309 5329-5330 5335-5343 5367-5368 5387-5391 5399-5401 5408-5410 5421-5425 5427-5429 5431-5433 5439 5455 5464-5466 5485 5490-5491
adult placenta	Clontech	APL001	313-315 491-492 605-606 719-722 736-740 834-835 950 971-979 1017-1022 1151-1153 1182-1184 1215-1216 1410 1418-1420 1532 1539-1540 1564-1566 1639 1719-1721 1747-1751 1870-1875 1925 1966-1974 1984 2101-2102 2230 2424 2510 2524-2525 2574-2575 2645-2647 2668 2818 2873-2874 3323-3324 3462 3483 4040-4042 4101-4102 4581-4582 4793-4795 5188-5189 5376
placenta	Invitrogen	APL002	12-13 192 364 491-492 520-521 709-711 755-757 789-793 840-844 885-886 975-979 1026-1027 1042-1043 1050 1070-1071 1076 1117-1119 1160-1164 1202-1207 1215-1216 1272-1273 1320-1321 1351 1360-1362 1380 1400-1401 1442-1443 1473 1553-1556 1564-1566 1603-1608 1621-1623 1694-1698 1724 1737-1739 1743-1745 1747-1751 1780-1783 1860 1948-1949 2062-2064 2072-2074 2101-2102 2111-2114 2146-2147 2186-2187 2204-2207 2310 2434-2435 2470-2472 2488 2511-2513 2594-2595 2645-2647 2677-2680 2696-2697 2737-2738 2831-2832 2836-2839 2899-2900 2925-2929 2954 3065-3067 3195 3199 3220-3222 3288 3313 3336-3338 3391 3403-3404 3466-3468 3536-3543 3624-3625 3638-3640 3932-3933 4082-4084 4273-4274 4291-4295 4410-4412 4701-4709 4740-4741 5431-5433 5435-5437
adult spleen	GIBCO	ASP001	78 137 154-156 175-177 213-215 274 278-283 313-315 324-325 332-333 341-344 346-349 420 456 479-480 491-492 511 530 557 612-620 652-653 659-660 677-678 699-701 728-733 741-744 764-771 784-786 814-816 822-823 849-851 924 944 950 964-966 975-988 994-995 997-998 1000-1002 1008-1009 1049 1052 1070-1071 1078 1088-1091 1128-1136 1151-1153 1171-1172 1193 1195-1196

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			1202-1204 1217-1218 1220-1221 1256 1269- 1271 1287 1294-1297 1315-1318 1332-1333 1349-1350 1352-1354 1359 1363-1371 1374 1383-1384 1386-1387 1397 1408-1409 1414 1418-1420 1422-1423 1425 1440-1441 1446- 1449 1486 1497 1507-1512 1514 1516-1517 1527-1532 1540-1548 1551-1552 1575-1576 1586-1589 1597 1603-1604 1612 1617-1619 1621-1623 1629-1632 1634-1637 1640-1645 1654 1656 1663 1686 1691-1692 1708 1710- 1714 1719-1721 1723-1724 1727 1737-1739 1746 1753 1765-1769 1773-1774 1780-1783 1796-1798 1807-1817 1827-1834 1853 1857- 1859 1870-1885 1903-1911 1913-1914 1919- 1922 1948-1949 1951 1964-1965 1978-1979 2025-2026 2035 2038 2040-2043 2045-2047 2054 2060-2061 2072-2074 2076-2079 2086- 2087 2111-2114 2116 2118 2131-2133 2137 2144 2148-2150 2153-2155 2178 2182-2183 2214-2215 2223 2230 2234-2242 2281-2283 2298-2299 2303-2304 2310 2331 2380-2382 2405-2413 2421 2440-2441 2452-2454 2456 2461 2469-2472 2488 2510-2513 2551 2560 2573 2603-2604 2608-2616 2650 2696-2697 2719-2720 2726 2747 2754-2758 2803 2818 2831-2832 2843-2845 2854 2861-2862 2873- 2874 2914-2917 2945-2946 2974-2976 3153 3158 3167-3168 3170-3171 3195 3210-3211 3215-3216 3226-3228 3250-3252 3258-3259 3280-3282 3289-3290 3336-3338 3385 3403- 3404 3428-3429 3466-3468 3536-3543 3561- 3562 3591-3593 3621-3625 3629-3630 3632- 3634 3716 3784-3786 3792 3815-3816 3878- 3879 3886 3935 3966-3971 4014-4015 4023 4036-4039 4060-4061 4077-4079 4090-4092 4098 4100 4126 4142-4143 4228 4232-4235 4239-4240 4335-4337 4374-4375 4400 4404- 4407 4451-4452 4554-4555 4598-4601 4622- 4623 4662 4668-4671 4740-4741 4796-4797 4832-4834 4864-4865 4907-4909 4912 4956- 4957 5001-5003 5034-5036 5074 5095-5097 5123-5124 5148-5149 5154-5157 5241-5242 5261-5267 5272-5274 5298-5302 5310-5311 5329-5330 5335-5343 5427-5429 5440-5441 5485
testis	GIBCO	ATS001	47 81-82 123 136 154-156 175-177 179 227- 230 278-283 313-315 341-344 366-367 379- 380 456 491-492 574-577 604 652-653 677- 678 682-684 699-701 743-744 764-771 784- 786 811-816 822-823 826-828 879-881 885-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Genomic DNA from BAC 63I18	Research Genetics (CITB BAC Library)	BAC001	3895
Genomic DNA from BAC 393I6	Research Genetics (CITB BAC Library)	BAC002	2639-2642

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
adult bladder	Invitrogen	BLD001	154-156 175-177 301-303 341-344 652-653 659-660 950 980-988 997-998 1042-1043 1069 1075 1139-1142 1160-1164 1193 1244-1246 1307 1508-1510 1575-1576 1717 1728-1734 1746 1805-1806 1870-1875 1882-1885 1903-1911 1981-1983 2004 2006-2007 2038 2060-2061 2072-2074 2118 2191-2192 2273 2283 2294-2295 2344 2639-2642 2721 2747 2818-2819 2914-2917 3112 3212 3280-3282 3424-3427 3470-3471 3536-3543 3664-3665 3691 3760 3791 3795-3800 4014-4015 4082-4084 4335-4337 4613 4796-4797 4864-4865 4960 5001-5003 5241-5242 5387-5388 5431-5433
bone marrow	Clontech	BMD001	30-31 42 48-50 74-78 114-115 120-123 137 143-165 175-177 213-215 227-230 232 235 278-290 297-303 305-309 313-315 324-325 335 341-344 354 379-380 394-398 435-438 440-441 447-455 462-471 491-492 513 516 520-521 538 551-553 557 561-562 641 652-653 661-671 674 677-678 680-684 699-701 709-760 763-772 794-795 822-823 849-851 857-859 863-869 882-886 889-897 909-914 916-918 921 924-926 931-936 944-945 950-956 969 980-988 992-995 997-1021 1026-1027 1032-1034 1038-1040 1049 1053-1055 1070-1071 1075 1079 1108 1110-1113 1128-1136 1139-1143 1151-1154 1173 1182-1184 1186-1187 1193 1198-1204 1217-1218 1220-1221 1228 1230-1232 1249-1256 1264 1269-1271 1274 1281-1282 1290-1291 1294-1297 1317-1319 1322-1345 1348-1362 1374-1379 1386-1387 1397-1399 1405-1407 1414-1417 1422-1423 1425 1437-1438 1440-1441 1444 1451-1464 1470 1479 1485-1489 1497-1500 1504-1505 1507-1512 1514-1515 1518-1520 1522-1526 1532-1563 1567-1576 1582-1585 1588-1589 1603-1608 1612 1621-1623 1625 1629-1632 1634-1637 1646-1648 1655-1656 1659-1660 1663-1664 1666-1670 1685-1690 1694-1698 1701-1702 1707-1708 1710-1716 1719-1721 1723-1724 1728-1739 1746 1752-1753 1755-1756 1765-1771 1773-1779 1805-1813 1830-1838 1853 1857-1860 1870-1875 1879-1881 1894-1896 1913-1922 1925-1936 1948-1951 1963 1966-1974 1978-1979 1993-1998 2000-2003 2005 2017-2020 2027-2030 2036-2056 2060-2064 2066-2067 2080-2082 2086-2087 2095 2098-2102 2107-2108 2111-2118 2121-2150 2153-2168 2172 2174-2177

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			2191-2195 2202-2203 2214-2221 2223 2229 2231-2242 2246-2248 2254 2262 2264 2273 2283 2288-2291 2294-2299 2302 2311-2312 2327-2330 2358 2377-2379 2387-2403 2418 2422-2424 2427 2440-2441 2443 2448-2465 2467-2469 2473-2474 2480 2488 2495 2510- 2513 2519-2520 2528-2531 2560 2572 2592 2598 2604 2628 2644-2648 2650 2656 2677- 2680 2686 2698-2699 2715 2719-2720 2722- 2744 2749-2750 2754-2758 2760-2761 2768- 2771 2774-2776 2781 2783 2785 2793-2820 2824-2826 2829 2843 2846-2847 2863-2867 2873-2874 2888 2891 2894-2895 2904-2905 2931-2939 2945-2946 2965-2973 2976 3008 3011-3012 3017-3022 3029 3041-3049 3054 3100 3102-3105 3150 3166-3175 3181-3186 3188-3194 3204 3208-3209 3212 3220-3222 3226-3230 3235-3243 3245-3252 3256-3273 3276-3277 3280-3283 3285 3289-3290 3299 3304-3307 3319-3322 3341-3346 3372-3373 3402 3406-3407 3422 3424-3427 3438-3441 3446-3449 3456 3466-3468 3470-3471 3486- 3487 3491-3495 3505-3506 3508-3513 3536- 3543 3550-3552 3557-3562 3566-3573 3576 3598-3607 3609-3614 3616-3628 3663-3665 3673-3677 3682 3707 3724-3725 3729-3730 3742-3744 3754 3761 3792 3794-3809 3817- 3821 3826 3828 3836-3861 3867-3869 3878- 3879 3881-3884 3897-3905 3911-3919 3955- 3957 3969-3971 4023 4028-4029 4052 4055- 4056 4082-4084 4094-4095 4101-4107 4109- 4120 4136 4142-4153 4156-4159 4167-4178 4208-4211 4215-4223 4227-4247 4267-4270 4275-4277 4285-4286 4291-4296 4383-4384 4430-4432 4494-4496 4501-4503 4517-4529 4531-4536 4554-4555 4572-4591 4596-4601 4624-4626 4649 4651 4662 4664-4665 4691- 4692 4729 4738-4741 4761-4780 4793-4810 4832-4834 4862-4865 4884 4907-4910 4923- 4928 4930-4931 4933-4935 4937-4943 4945 4961-4985 5001-5003 5038-5039 5050-5052 5080 5114-5115 5137-5141 5148-5149 5153- 5157 5180 5190-5192 5241-5242 5250 5252 5254-5277 5303-5305 5307-5325 5327-5343 5345-5354 5367-5374 5376-5379 5381-5385 5387-5388 5397-5398 5444 5460-5461 5464- 5466 5485
bone marrow	Clontech	BMD002	175-177 249-250 254 258-260 301-303 313- 315 324-325 413-414 440-441 491-492 540 574-577 580-581 592-594 599-601 612-620

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			652-653 724-733 741-750 804-805 814-816 846 849-851 889-897 903-905 910-914 957- 960 970 992 994 997-998 1010-1014 1023- 1027 1038-1040 1089-1091 1095 1110-1113 1128 1202-1207 1217-1218 1235-1236 1256 1271 1297 1319 1330-1333 1348-1350 1352- 1354 1357-1358 1383-1384 1397 1457-1462 1479 1491-1494 1497 1504 1507-1512 1532 1547-1548 1551-1552 1575-1576 1621-1623 1646-1647 1686 1719-1721 1727 1743-1745 1753-1754 1763-1764 1773-1779 1796-1798 1805-1806 1814-1817 1827-1830 1839-1844 1848-1851 1913-1918 1925 1993-1998 2040- 2043 2048 2052-2054 2060-2061 2078-2079 2088-2091 2116-2118 2131-2142 2148-2150 2172 2174-2176 2191-2195 2223 2246-2248 2318-2320 2537-2538 2553 2604 2638 2702- 2705 2709-2711 2713-2714 2739 2781 2796- 2798 2803 2931-2939 2961-2962 3026-3027 3055 3130 3159-3162 3181-3183 3246 3250- 3252 3304-3307 3402 3536-3543 3793 3847- 3849 3925-3926 4024-4025 4060-4061 4209- 4210 4228 4252-4253 4267-4270 4574 4581- 4582 4729 4787 4796-4797 4858 4907-4909 4974 4991-4993 5021-5023 5050-5052 5056 5148-5149 5260-5267 5272-5275 5278-5279 5335-5343 5377-5378 5416 5423-5425 5485
bone marrow	Clontech	BMD004	728-733 849-851 1349-1350 1486 1860 2050- 2051 2134-2136 2148-2150 2234-2242 2803 4209-4210 4598-4601 4652-4653 4907-4909 5261-5267 5272-5274
bone marrow	Clontech	BMD007	396-398 440-441 453-455 491-492 712-718 764-771 814-816 846 849-851 1096-1104 1146-1147 1315-1316 1486 1497 1522-1523 2134-2136 2148-2150 2223 2803 3250-3252 4598-4601 5001-5003 5050-5052 5310-5311
adult colon	Invitrogen	CLN001	1-2 32-34 64 175-177 251 278-283 452 478 814-816 832 870 889-897 944 957-960 1044- 1047 1069 1117-1119 1128 1139-1142 1195- 1196 1217-1218 1317-1318 1386-1387 1511- 1512 1547-1548 1640-1645 1709 1770-1771 1860 1870-1875 1882-1885 1948-1949 1952- 1953 1981-1983 2088-2091 2146-2147 2156- 2160 2174-2176 2208-2210 2254 2347-2348 2511-2513 2604 2629-2631 2737-2738 2831- 2832 2852-2853 2865 3035-3036 3156-3157 3220-3222 3246 3339-3340 3554-3556 3632- 3634 3663 3673-3677 3693 3780-3781 3870 3949-3951 4272 4275-4277 4330-4331 4534 4636-4637 4651 4668-4674 4776 4796-4797

<b>Tissue origin</b>	<b>RNA Source</b>	<b>Library Name</b>	<b>SEQ ID NOS:</b>
Mixture of 16 tissues – mRNAs*	Various Vendors*	CTL016	210-211 910-914 995 1128 1479 1617-1619 1626 1784-1790 1913-1914 2901-2903 2979 3831-3833 4796-4797 5001-5003 5075-5077 5154-5157 5414-5415
Mixture of 16 tissues – mRNAs*	Various Vendors*	CTL021	175-177 237-240 652-653 801-803 849-851 950 993 1042-1043 1063-1067 1156 1310-1314 1332-1333 1485 1511-1512 1533-1535 1746 2148-2150 2182-2183 2186-2187 2223-2228 2233 2253 2484-2485 2843 2979 3189-3191 3250-3252 4796-4797 4907-4909 5001-5003 5050-5052 5196 5226
adult cervix	BioChain	CVX001	1-2 32-34 52 56 70 107-110 123 125 133-134 137 140-142 153-156 175-177 195-196 212 227-230 233 278-283 288-290 301-303 313-315 324-325 335 341-344 365 379-380 394 396-398 491-492 514 520-521 539 583-590 597-598 611 682-684 697 699-701 708 719-722 810 814-816 822-823 840-844 857-859 863-870 873-875 879-881 885-886 889-897 899 903-905 909 915 919-920 925-926 931-936 950-953 957-962 975-988 992-995 997-998 1000-1002 1022 1032-1034 1044-1047 1049 1052 1069 1075 1110-1113 1129-1130 1144-1145 1154-1155 1165-1170 1172-1173 1182-1184 1198-1204 1215-1216 1220-1221 1256 1263 1271 1287 1297 1300-1301 1319-1321 1323-1328 1352-1355 1360-1371 1374 1397 1400-1401 1410 1413 1421 1440-1444 1455-1464 1470 1475-1477 1479-1480 1487 1491-1494 1504 1507-1510 1515-1517 1524 1547-1548 1551-1552 1557 1569-1574 1599-1608 1611 1620 1625 1639 1648 1653-1654 1657-1658 1663 1683-1685 1690 1715-1716 1723 1735-1736 1753-1756 1763-1764 1780-1783 1792-1795 1805-1806 1827-1829 1835-1844 1852 1870-1877 1879-1881 1896 1925-1927 1951 1964-1965 1993-1998 2000-2002 2005 2021-2024 2031-2035 2038 2042-2043 2048 2050-2056 2058-2059 2062-2064 2066-2067 2072-2074 2078-2079 2086-2087 2096-2100 2111-2114 2116 2118 2137 2143-2144 2146-2147 2156-2160 2177-2181 2191-2192 2216-2221 2223-2228 2234-2242 2249 2251-2252 2254-2257 2273 2275 2277 2280-2282 2296-2299 2302 2327-2331 2333-2334 2341 2344 2349-2356 2358 2368 2377-2381 2389-2390 2423-2424 2456 2467 2483 2490-2494 2499 2510-2513 2546 2549-2550 2560 2563 2573-2575 2591 2594-2595 2597 2603-2604 2628-2631 2645-2647 2651-2655 2706 2713-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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diaphragm	BioChain	DIA002	574-577 1230-1232 1524 1605-1608 2116 2143 2843 3795-3800 4060-4061 4598-4601
endothelial cells	Stratagene	EDT001	1-2 32-34 38 45-46 56 70 74-77 137 140-142 165 173 175-177 187-190 195-196 213-215 220 231 278-283 294-295 313-315 330 332- 333 341-344 346-349 364 366-367 379-380 395 445-446 474 491-495 511 520-521 531- 532 545 548-553 574-577 612-620 652-653 682-684 697 704-706 709-711 719-722 801- 803 811-816 822-823 836-837 863-872 879- 881 885-886 889-897 899 903-914 919-920 927 930-936 944 950 954-962 964-966 969 971-988 993-995 997-998 1000-1002 1007- 1014 1017-1021 1026-1027 1032-1034 1036- 1040 1042-1052 1068-1071 1075-1076 1079 1089-1091 1095 1110-1113 1117-1119 1128- 1136 1139-1143 1151-1153 1155-1156 1160- 1164 1172 1192-1193 1198-1204 1217-1218 1220-1221 1235-1242 1244-1246 1249-1255 1281-1282 1287 1294-1297 1300-1301 1315- 1319 1328 1337-1345 1349-1355 1357-1359 1374 1380 1386-1387 1390-1393 1397-1401



Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Genomic clones from the short arm of chromosome 8	Genomic DNA from Genetic Research	EPM001	2639-2642
esophagus	BioChain	ESO002	885-886 1639 2223
fetal brain	Clontech	FBR001	153 278-283 863-869 1156 1400-1401 1626 1691-1692 1727 2118 2229 2604 2645-2647 2844-2845 3174 3763 3780-3781 4090-4092 4140-4141 4545 4835
fetal brain	Clontech	FBR004	855-856 1017-1021 1470 1580-1581 1839- 1844 1978-1979 2052-2053 2084 2171 2249 3197 3451-3455 3713 4960
fetal brain	Clontech	FBR006	30-31 39-40 74-77 116-119 130 137 143-148 175-177 187-190 195-196 216-218 223-226 366-367 388-390 400-404 465 491-492 520- 521 557 602-603 607 647-649 652-653 670- 671 676 680-681 685 698 724-727 743-744 760 763 789-793 814-817 824-825 829-831 836-837 849-851 855-856 885-886 889-897 944 994 997-998 1000-1002 1017-1021 1026- 1027 1042-1043 1068-1069 1076 1089-1091 1095 1139-1142 1151-1153 1156 1176 1182- 1185 1192 1220-1221 1228 1230-1232 1332- 1333 1349-1350 1357-1358 1389 1394 1400- 1401 1403-1404 1408-1409 1413 1455-1456 1507-1510 1520 1605-1608 1617-1619 1629-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal brain	Clontech	FBRs03	1870-1875 1878 3424-3427 3554-3556 4907-4909 5137-5140
fetal brain	Invitrogen	FBT002	32-34 59-60 92-96 124 128 137 180-182 192 195-196 278-283 341-344 436 491-492 520-521 583-590 607 647-649 652-653 677-678 778-783 789-793 822-825 849-854 882-884 950 957-960 964-966 971-974 980-988 1026-1028 1038-1040 1042-1043 1050 1070-1071 1076 1127 1156 1205-1207 1230-1232 1271 1281-1282 1322 1337-1345 1349-1350 1360-1371 1386-1387 1400-1401 1414-1417 1427-1431 1435-1436 1470 1507-1510 1532 1603-1604 1617-1620 1633 1649-1653 1674-1682 1691-1692 1694-1698 1708 1710-1714 1727 1737-1739 1765-1769 1773-1774 1780-1783 1805-1806 1839-1844 1852 1870-1875 1882-1885 1896 1925 1964-1965 1978-1979 1990-1991 1993-1998 2031-2034 2058-2059 2084 2109-2110 2118 2173 2186-2187 2193-2195 2202-2203 2208-2210 2233 2254 2278 2288-2291 2305-2306 2414-2415 2496 2511-2513 2537-2538 2558-2559 2573 2579-2584 2590 2597 2604 2629-2631 2639-2642 2659-2662 2672-2674 2696-2697 2719-2720 2741-2743

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal heart	Invitrogen	FHR001	909 1089-1091 1128 1256 1514 1621-1623 3354 4228
fetal kidney	Clontech	FKD001	30-31 137 154-156 212 278-283 313-315 326-327 370-371 379-380 491-492 551-553 595 602-604 665-667 680-681 736-740 743- 744 822-823 900-902 950-956 995 1023-1025 1035 1085 1089-1091 1182-1184 1230-1232 1300-1301 1332-1333 1353-1354 1357-1359 1386-1387 1446-1449 1457-1462 1479 1515 1532 1551-1552 1580-1581 1588-1589 1612 1617-1619 1629-1632 1663 1667-1670 1719- 1721 1724 1746 1752-1754 1796-1798 1831- 1834 1845-1847 1896-1897 1925-1927 1951 1981-1983 1993-1998 2035 2045-2047 2111- 2114 2118 2144 2224-2228 2253 2360 2422 2440-2441 2502 2510 2526-2527 2549-2550 2645-2647 2650 2693 2763 2774-2776 2781 2831-2832 2844-2845 2879-2881 2898 2913 2960 2974-2975 2979 3031-3032 3054 3198 3230 3276-3277 3304-3307 3372-3373 3442 3446-3449 3491-3495 3536-3543 3714 3780- 3781 3853 4030-4031 4055-4056 4093 4581- 4582 4679 4864-4865 4907-4910 5001-5003 5038-5039 5050-5052 5142-5143 5148-5149 5329-5330 5372-5374
fetal kidney	Clontech	FKD002	313-315 551-553 699-701 743-744 784-786 1017-1021 1173 1182-1184 1403-1404 1753 2055-2056 2116 2118 2223 2253 4598-4601 4907-4909 5001-5003
fetal kidney	Invitrogen	FKD007	45-46 491-492 849-851 950-953 1507 1575- 1576 1746 2060-2061 2086-2087 2134-2136 2204-2207 2223-2228 2380-2381 2579-2584 3242 4581-4582
fetal lung	Clontech	FLG001	64 350-352 453-455 551-553 736-740 822- 823 863-869 997-998 1000-1002 1035 1042- 1043 1193 1275-1277 1317-1318 1374 1648 1674-1682 1707 1727 1746 1753 1830 1835- 1844 1852 1870-1875 1951 2004 2066-2071

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal lung	Invitrogen	FLG003	195-196 278-283 341-344 388-390 395 450-451 491-492 849-851 879-881 885-886 950 971-979 995 1128 1193 1237-1242 1269-1270 1386-1387 1450 1507 1514 1605-1608 1709 1746 1780-1783 1830 1835-1838 1848-1852 1860 1865-1875 1990-1991 2010-2013 2060-2061 2072-2074 2094 2174-2176 2233 2253 2283 2526-2527 2579-2584 2594-2595 2836-2839 2844-2845 2888 2896-2897 2913 2951-2952 2979 2985 3008 3123 3149 3200-3202 3212 3258-3259 3280-3282 3466-3468 3508-3513 3536-3543 3605 3629-3630 3691 3749-3752 3793 3840-3841 4016-4018 4114-4116 4258 4330-4331 4598-4601 4897 5102-5104 5119 5276-5277
fetal lung	Clontech	FLG004	154-156 971-974 1070-1071 1182-1184 1527-1531 1701-1702 1753 1896 3462 3629-3630 5001-5003 5241-5242
fetal liver-spleen	Columbia University	FLS001	1-13 24-27 29-50 52-99 111-113 115 126 133-134 136 140-142 154-156 166-192 195-222 227-230 232-236 241-283 286-287 291 307-310 313-327 330-334 336-361 365-367 369-375 379-383 386-394 396-420 422-431 435-446 453-456 461 474-475 478-481 483-505 507-532 534-545 548-553 557 561-562 565-567 569-577 580-581 583-607 611-620 629-631 633-650 652-653 655-662 682-684 699-701 704-706 709-711 724-727 736-740 743-744 747-750 755-759 773-829 832-835 839-854 857-877 882-886 889-905 909-921 924 927-966 968-969 971-988 990-995 997-1014 1017-1050 1052-1055 1058-1059 1063-1074 1076 1078-1082 1085-1088 1092 1094 1096-1104 1107-1108 1110-1113 1115-1121 1124 1127-1145 1148 1150-1175 1177-1223 1225-1256 1263-1289 1292-1301 1307-1327 1332-1335 1337-1345 1349-1350 1352-1355 1357-1371 1374-1379 1386-1387 1389-1393 1395-1397 1400-1401 1403-1406 1408-1410 1414-1423 1425 1432 1434 1437-1438 1440-1444 1446-1462 1467-1473 1479-1480 1485-1486 1495-1500 1504 1507-1510 1513-1514 1518-1519 1522-1524 1527-1538 1540-1548 1551-1557 1559-1576 1579-1608 1611-1623

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal liver-spleen	Columbia University	FLS002	3-11 24-27 35 38 42 44 48-50 57 67 70 73-77 85 88 98 107-111 136-142 151-153 165 173 195-196 198 201-205 210-215 219 222 232- 234 236 245 252-254 258-266 277 291 316- 320 332-333 337 354 357-361 365 374-375 381-383 394 406 415-416 418 436-438 445- 446 461 478-480 486 489-490 520-521 527 538 540 543 548-553 574-577 599-601 607 612-620 647-649 677-678 682-685 699-706 709-711 736-740 747-750 755-759 777 788- 793 814-816 818 822-828 833 852-854 863- 869 873-877 885-886 889-897 899-902 906- 914 916-920 924 927-936 946-949 951-956 961-962 969 975-988 990-991 993-995 999- 1014 1023-1037 1041-1047 1052 1055 1063- 1067 1070-1071 1076 1080 1085 1088 1108 1110-1119 1124 1128-1142 1144-1145 1148 1151-1156 1158 1160-1170 1172-1175 1177- 1184 1186-1187 1192-1193 1195-1197 1202- 1204 1208-1212 1215-1218 1220-1221 1225- 1227 1235-1236 1244-1246 1249-1256 1263 1266-1273 1278-1280 1285-1291 1297-1301 1307 1315-1316 1320-1327 1332-1333 1349- 1350 1352-1355 1357-1371 1374-1379 1385- 1387 1389 1395-1397 1405-1406 1410 1414- 1417 1421-1423 1425 1427-1432 1437 1442- 1444 1451-1456 1463-1464 1470-1473 1475- 1477 1479-1480 1485 1498-1499 1515 1536- 1538 1540-1546 1550-1557 1559-1560 1580- 1585 1597 1603-1608 1612-1616 1620 1625- 1627 1629-1632 1638-1653 1656 1661-1662 1664 1667-1682 1685 1691-1692 1694-1699 1701-1704 1706-1707 1709-1714 1717 1719-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal liver-spleen	Columbia University	FLS003	210-211 341-344 849-851 1089-1091 1177-1179 1310-1314 1320-1321 1349-1350 1440-1441 1514 1557 1624 1648 2042-2043 2134-2136 2223 2253-2254 2511-2513 2533 2843 2979 4163-4166 4273-4274 4687-4689 4738-4739 4998-4999 5075-5077 5414-5415 5452-5453
fetal liver	Invitrogen	FLV001	3-11 52 246-247 255-260 278-283 291 341-344 491-492 596 652-653 709-711 724-727 778-783 814-816 840-844 849-851 882-886 903-905 946-949 964-966 971-988 997-998 1003-1006 1010-1014 1026-1027 1038-1040 1044-1047 1063-1068 1070-1071 1089-1091 1137-1138 1143 1171 1177-1179 1182-1184 1193 1198-1201 1205-1207 1310-1314 1317-1318 1320-1321 1337-1345 1349-1350 1360-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal liver	Clontech	FLV002	1411 1605-1608 1625 4581-4582 5323-5325
fetal liver	Clontech	FLV004	210-211 258-260 313-315 652-653 852-854 863-869 971-974 1116 1128 1171 1177-1179 1182-1184 1192 1205-1207 1374 1422-1423 1605-1608 1613-1616 1626 1648 1701-1702 1725-1726 1775-1779 1913-1914 2116 2134- 2136 2188 2223 2253 2484-2487 2677-2680 3076-3078 3328-3330 4451-4452 4777-4780 4998-4999 5050-5052 5082-5083 5310-5311 5387-5388 5414-5415
fetal muscle	Invitrogen	FMS001	3-11 154-156 216-218 278-283 313-315 341- 344 388-390 395 478 491-495 511 591 652- 653 704-706 814-816 822-823 889-897 903- 908 925-926 928-929 931-936 946-950 957- 960 980-988 993 1017-1021 1048-1050 1063- 1068 1171 1297-1299 1307 1320-1321 1359 1444 1507-1510 1514 1533-1535 1540 1553- 1556 1585 1605-1608 1639 1694-1698 1710- 1714 1717 1746 1753 1773-1774 1780-1783 1805-1813 1860 1879-1885 1915-1918 2004 2042-2043 2107 2118 2134-2136 2148-2150 2161-2162 2197-2199 2254-2257 2281-2282 2503-2504 2665 2686 2824-2826 2843 2852- 2853 2896-2897 2979 2985 3054 3058-3059 3159-3162 3213-3214 3226-3228 3280-3282 3299 3323-3324 3365-3366 3372-3373 3658-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal muscle	Invitrogen	FMS002	341-344 652-653 1298-1299 1389 1400-1401 1507 1727 1746 1753 2042-2043 2191-2192 2224-2228 2761 2979 3123 3257 4285-4286 4410-4412
fetal skin	Invitrogen	FSK001	1-2 39-40 70 92-95 137 157-159 175-177 213-215 246-247 278-283 291 298-300 313- 315 341-344 365 370-371 388-390 419 445- 446 452 478-480 511 516 522-524 538-539 548-553 580-581 597-598 602-603 633-634 647-649 652-653 677-678 685 709-711 784- 786 789-793 814-816 824-829 849-851 863- 870 879-884 903-905 909 919-920 925-926 946-949 957-960 980-988 992-994 997-1002 1010-1014 1017-1021 1035 1042-1047 1050- 1051 1076 1078 1110-1113 1117-1119 1129- 1130 1151-1155 1160-1164 1182-1184 1198- 1204 1237-1243 1256 1271 1290-1291 1307 1310-1314 1320-1321 1323-1327 1351 1355 1357-1359 1380 1385 1390-1393 1400-1401 1414 1418-1420 1432 1435-1436 1450 1457- 1462 1479 1488-1489 1507-1510 1524 1533- 1535 1547-1548 1550-1552 1567-1568 1575- 1576 1579 1585 1588-1589 1611 1617-1619 1621-1623 1653-1655 1663 1686 1688-1689 1691-1692 1694-1698 1703-1704 1710-1714 1743-1746 1753 1765-1771 1773-1774 1780- 1783 1807-1813 1830-1834 1848-1852 1865- 1878 1882-1885 1903-1911 1915-1918 1925- 1927 1954-1962 1964-1965 1981-1983 1990- 1991 2006-2007 2017-2030 2038 2054 2068- 2071 2076-2079 2088-2091 2098-2100 2107 2118 2145 2153-2155 2173 2177 2179-2181 2188 2191-2192 2204-2210 2214-2215 2246- 2248 2251-2253 2267-2271 2277 2280 2286- 2291 2305-2306 2310 2338-2340 2376 2386 2432 2434-2435 2437 2469 2483 2490-2491 2510-2513 2526-2527 2560 2563 2572-2573 2588-2589 2594-2595 2603 2628 2659-2662 2696-2697 2734 2741-2743 2754-2758 2782 2787-2789 2813 2819 2824-2826 2828 2831- 2832 2843-2845 2855-2860 2865 2873-2874 2905 2914-2917 2925-2929 2945-2946 2951- 2952 2955 2961-2962 2965-2975 2979 2981- 2983 2985 2989 2996-2998 3000 3008 3023 3082 3109-3110 3151-3153 3156-3157 3167- 3168 3195 3213-3216 3220-3222 3234 3247-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal skin	Invitrogen	FSK002	313-315 341-344 366-367 551-553 971-974 1038-1040 1151-1153 1271 1353-1354 1507-1510 1588-1589 1755-1756 1870-1875 1903-1911 1926-1927 1952-1953 2017-2020 2027-2030 2078-2079 2197-2199 2377-2379 2669-2671 2677-2680 2931-2939 3167-3168 3189-3191 4082-4084 4613 4907-4909 5423-5425
fetal spleen	BioChain	FSP001	175-177 743-744 1171 1202-1204 1457-1462 1753 2060-2061 2116 2143 2223 2253 2728-2729 4167-4168 5001-5003 5335-5343 5444
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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fetal brain	GIBCO	HFB001	3-11 32-34 39-40 42 78 81-82 100-110 116- 119 124-142 154-156 165 175-177 195-196 201-205 212-218 220 278-283 286-287 291- 296 313-315 335 341-344 346-349 366-367 379-380 388-390 396-398 419 456-461 491- 492 511 551-553 557 561-562 574-577 583- 590 651-653 676-679 682-694 697-711 743- 744 784-786 804-805 814-816 822-825 848- 851 855-859 863-869 871-872 882-884 899- 902 915-918 927 930-936 944-945 951-953

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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macrophage	Invitrogen	HMP001	244 278-283 440-441 445-446 794-795 855-856 995 999 1017-1021 1353-1354 1507 1582-1584 2223 4228 4864-4865 5490-5491
infant brain	Columbia University	IB2002	32-35 39-40 45-47 64 70 74-77 81-82 92-95 100-110 116-119 124 126 136 154-156 175-177 180-182 195-196 213-218 227-230 246-247 254 278-283 291 296 340 346-352 362 364-365 388-390 413-414 419 445-446 459 491-492 509 511 551-553 574-577 579-590 592-594 607 652-653 675-676 680-681 743-744 755-757 789-793 796 806-808 824-825 832 849-851 855-859 863-872 900-918 924 927 944 951-956 964-966 971-988 990-995 997-998 1008-1009 1022 1026-1027 1036-1040 1042-1043 1049-1054 1069-1071 1088-1091 1110-1113 1117-1121 1127 1129-1130 1139-1143 1154-1155 1159 1172-1173 1175 1180-1181 1192-1193 1198-1207 1217-1218 1220-1221 1230-1232 1235-1236 1256 1263 1274 1281-1282 1290-1291 1297 1300-1301 1307 1315-1316 1319-1321 1328 1334-1335 1349-1350 1357-1359 1363-1371 1394-1399 1402-1404 1410-1411 1413-1420 1422-1424 1427-1431 1437 1439-1441 1444 1451-1462 1465-1470 1479 1485 1498-1499 1507-1510 1540 1547-1548 1550-1552 1580-1584 1586-1587 1592 1603-1608 1617-1620 1638-1639 1646-1648 1653 1656 1664-1673 1693-1699 1719-1721 1727-1734 1737-1739 1743-1745 1752-1756 1763-1769 1773-1774 1780-1783 1805-1806 1814-1817 1830-1834 1848-1852 1865-1885 1896-1897 1899 1903-1911 1926-1927 1951-1962 1964-1974 1978-1979 1990-1991 2000-2003 2010-2013 2017-2020 2025-2030 2052-2056 2058-2061 2066-2067 2092 2098-2100 2131-2133 2138-2144 2151-2152 2161-2162 2171 2177 2186-2190 2200-2201

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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infant brain	Columbia University	IBM002	133 491-492 682-684 743-744 889-897 1038- 1040 1427-1431 1474 1580-1581 1633 1903- 1911 2025-2026 2146-2147 2188 2310 2376 2726 2787-2789 2904 2992 3212-3214 3224- 3225 3325 3477-3478 3638-3640 3827 3966- 3968 4055-4056 4118 4131 4275-4277 4643 5044
infant brain	Columbia University	IBS001	153 197 350-352 459 574-577 743-744 826- 828 871-872 903-905 969 995 997-998 1042- 1043 1068 1127 1151-1153 1287 1349-1350 1559-1560 1694-1698 1773-1774 1848-1851 1978-1979 2054-2056 2111-2114 2143 2200- 2201 2365 2521 2664 2707-2708 2843 2945- 2946 2978 3260-3267 3424-3427 3599-3601 3624-3625 3737-3738 3891 4114-4116 4125 4245 4291-4295 4635 4907-4909
lung, fibroblast	Stratagene	LFB001	137 313-315 435 491-492 579 822-823 885- 886 910-914 944 950 961-962 994-995 997- 998 1000-1002 1026-1027 1049-1050 1052 1068 1075 1079 1110-1113 1129-1130 1143 1172 1182-1185 1192 1202-1204 1266-1267 1274 1287 1294-1296 1298-1299 1307 1315- 1318 1351 1374 1395-1396 1400-1401 1407 1411 1418-1420 1444 1455-1456 1473 1485 1507 1516-1517 1532-1535 1547-1548 1553-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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lung tumor	Invitrogen	LGT002	32-34 42 45-46 67 96 100-106 116-120 136- 139 153 175-177 179 195-196 213-218 227- 230 278-283 298-300 313-315 324-325 332- 333 341-344 346-349 357-361 365 379-380 393-394 400-404 420 436 474 478 483-485 491-492 513-514 538 548-550 557 574-577 580-581 605-607 611 652-653 682-684 699- 701 709-711 723 728-733 743-744 764-771 778-783 799-803 840-844 852-854 857-859 873-875 885-886 889-897 909-920 924 946- 956 964-966 969 971-979 992-995 997-1006 1008-1009 1023-1027 1036-1040 1042-1043 1048-1050 1063-1067 1088-1091 1110-1113 1117-1119 1128-1130 1139-1143 1151-1153 1155-1156 1160-1164 1172-1173 1185 1193 1202-1212 1217-1218 1220-1221 1229-1232 1235-1236 1244-1246 1269-1271 1300-1301 1315-1318 1323-1328 1330-1333 1349-1355 1357-1359 1363-1371 1374 1397 1403-1404 1408-1409 1418-1423 1432 1434 1438 1440- 1441 1446-1449 1463-1464 1467-1470 1473 1480 1491-1494 1505 1507-1512 1533-1535 1541-1548 1550-1557 1569-1574 1585 1591 1611-1612 1617-1619 1621-1623 1625 1629- 1632 1639-1645 1648 1654-1655 1657-1660 1663-1664 1671-1673 1685 1687-1689 1691- 1692 1694-1698 1706-1707 1710-1716 1719- 1721 1727-1739 1743-1746 1763-1771 1780-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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leukocyte	GIBCO	LUC001	1-2 12-22 39-40 45-47 70 78 107-110 135- 136 154-156 165 175-177 212-215 223-226 231 258-260 267-268 278-283 286-287 313- 315 324-325 332-333 341-344 364 379-380 388-390 394-395 415-416 419 437-438 450- 451 456 462 465 478-480 491-492 511 520- 524 531-532 538 551-553 557 561-562 574- 577 583-590 597-598 602-603 612-620 633- 634 641 652-653 668-669 677-685 699-701 704-711 719-722 728-733 743-744 754-757 760 763-771 784-786 794-796 811-816 822- 828 840-844 847 849-851 855-856 879-886

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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leukocyte	Clontech	LUC003	1-2 48-50 154-156 195-196 286-287 313-315 324-325 395 520-521 557 602-603 772 784- 786 814-816 822-823 863-869 885-886 906- 908 944 954-956 963 980-988 995 1050 1080 1122 1129-1130 1182-1184 1192 1198-1201 1317-1319 1348-1350 1353-1355 1357-1358 1374 1432 1450 1507 1516-1517 1532-1535 1547-1548 1664 1686 1715-1716 1737-1739 1753 1814-1817 1857-1859 1888-1893 1903- 1911 1919-1922 1950 1984 2010-2013 2035 2038 2054 2058-2061 2116 2118 2125-2133 2178 2191-2192 2223 2278 2572 2574-2575

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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melanoma from cell line ATCC #CRL 1424	Clontech	MEL004	1-2 52 96 138-139 278-283 313-315 479-480 491-495 511 799-800 822-823 829 847 863- 869 871-875 889-897 944 951-953 957-962 980-988 993 1017-1021 1038-1040 1042- 1043 1129-1130 1172-1173 1182-1184 1202- 1204 1220-1221 1237-1242 1269-1270 1290- 1291 1337-1345 1359 1400-1401 1403-1404 1432 1435-1436 1438 1442-1443 1457-1464 1475-1477 1489 1505 1507 1524 1532 1536- 1538 1547-1548 1551-1556 1575-1576 1585 1603-1604 1611 1617-1619 1648 1663 1688- 1689 1691-1692 1701-1702 1715-1716 1719- 1721 1724 1735-1736 1746 1755-1756 1780- 1783 1845-1847 1876-1877 1882-1885 1925 1954-1962 1981-1983 2005 2045-2047 2058- 2061 2088-2091 2115 2118 2138-2142 2144 2178 2189-2190 2197-2199 2223 2254 2266 2277 2281-2282 2284 2298-2299 2310 2347- 2348 2389-2390 2418 2424 2427 2440-2441 2443 2510-2513 2548 2591 2597 2637 2659- 2662 2781 2783 2814 2824-2826 2843-2845 2857-2860 2898 2905 2945-2946 2955 2969- 2973 3008 3029 3094-3095 3130 3166 3170- 3173 3195-3196 3226-3228 3240 3258-3259 3339-3340 3438-3441 3443 3459-3460 3574- 3575 3577-3580 3589 3599-3601 3635 3658- 3660 3691 3753 3815-3816 3828 3878-3879 3941-3942 3966-3968 4077-4079 4104-4105 4121-4122 4132-4133 4142-4144 4241-4242 4275-4277 4287-4288 4326 4391-4393 4546- 4548 4672-4674 4679 4737 4796-4797 4835 4902 5055 5057-5065 5085-5088 5280 5308- 5309 5389-5391 5421-5422
mammar y gland	Invitrogen	MMG001	1-2 12-13 39-40 47 62 81-82 96 116-119 126 173 175-177 180-182 195-196 213-215 227- 230 236 246-247 258-260 274 278-283 313- 315 321 341-344 346-349 354 365-367 399 419-420 445-446 450-451 478 491-492 520- 521 538 543 580-581 583-590 602-603 607 629-630 647-649 652-653 670-671 677-678 682-684 697 709-711 728-733 743-744 764- 771 789-793 796 801-803 806-808 814-816 840-844 870 879-881 885-886 900-905 909-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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<b>Tissue origin</b>	<b>RNA Source</b>	<b>Library Name</b>	<b>SEQ ID NOS:</b>
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induced neuron cells	Strategene	NTD001	313-315 548-553 682-684 814-816 903-905 909 944 950 969 993 1017-1021 1026-1027 1036-1037 1070-1071 1088 1285 1294-1296 1315-1316 1322 1357-1358 1363-1371 1403- 1404 1520 1536-1538 1620 1629-1632 1638 1663 1701-1702 1707-1708 1724 1753 1770- 1771 1915-1918 1925-1927 1950 1993-1998 2017-2020 2025-2026 2058-2061 2083 2121- 2124 2144 2151-2152 2197-2199 2331 2386 2469 2573 2596 2628 2752-2753 2843 2898 2925-2929 2961-2962 2969-2973 3172-3173 3189-3191 3224-3225 3253-3255 3310-3311 3428-3429 3470-3471 3673-3677 3760 3969- 3971 4014-4015 4082-4084 4090-4092 4100 4114-4116 4140-4141 4272 4285-4286 4470 4616-4621 4691-4692 4761-4763 4864-4865 4907-4909 5137-5140 5298-5302
retinoic acid induced neuronal cells	Strategene	NTR001	195-196 278-283 388-390 743-744 855-856 995 1038-1040 1139-1142 1418-1420 1533- 1535 1780-1783 1903-1911 2060-2061 2223 2592 3289-3290 3969-3971 4598-4601
neuronal cells	Stratagene	NTU001	74-77 195-196 246-247 278-283 294-295 341-344 388-390 491-492 566 652-653 680- 681 743-744 755-757 784-786 801-803 855- 856 863-869 900-902 919-920 950 964-966 995 997-998 1000-1002 1076 1159 1235- 1236 1294-1297 1432 1451-1454 1507 1533- 1535 1605-1608 1648 1667-1670 1688-1689 1691-1692 1694-1698 1703-1704 1746 1753 1765-1769 1831-1834 1848-1851 1900-1902 1925 1966-1974 2060-2061 2088-2091 2095

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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pituitary gland	Clontech	PIT004	175-177 227-230 491-492 796 822-823 849-851 992 995 1017-1021 1042-1043 1160-1164 1182-1184 1202-1204 1215-1216 1220-1221 1300-1301 1317-1318 1320-1321 1398-1399 1410 1479 1507 1540 1553-1556 1582-1585 1591 1625 1648 1657-1658 1663 1708 1753 1870-1875 1925 2060-2061 2068-2071 2118 2447 2604 2696-2697 2715 2774-2776 2843 2871-2872 3021-3022 3100 3203 3331-3332 3339-3340 3424-3427 3577-3580 3684 3787-3788 3959-3960 4549 5431-5433
placenta	Clontech	PLA003	1052 1215-1216 1694-1698 1919-1922 2116 3969-3971 4672-4674 5001-5003 5241-5242
prostate	Clontech	PRT001	42 165 246-247 335 511 548-550 675 847 873-875 879-881 889-897 910-914 946-949 980-988 993 995 1008-1009 1038-1040 1049 1128 1154 1157 1173 1182-1184 1202-1204 1297 1317-1318 1352 1357-1359 1398-1399 1414 1457-1462 1485 1498-1499 1524 1553-1556 1629-1632 1648 1683-1684 1688-1689 1718-1721 1746 1753 1770-1771 1792-1795 1831-1834 1860 1870-1875 1879-1881 1925-1927 1990-1991 2005 2035 2038 2045-2047 2055-2056 2060-2064 2083 2088-2091 2118 2144 2179-2181 2202-2203 2229 2254 2277 2283 2296-2297 2303-2304 2315 2337-2340 2387 2418 2423 2427 2445 2456 2468 2475 2492-2495 2510 2536 2543-2544 2546 2549-2550 2574-2575 2591-2592 2604 2645-2647 2649 2659-2662 2712 2721 2749-2750 2760 2857-2860 2871-2872 2894-2895 2909-2911 2925-2929 2951-2952 3005 3013-3014 3017-3020 3029 3081 3100 3121 3148 3174 3199 3226-3228 3242 3250-3252 3276-3277 3280-3282 3558-3560 3606-3607 3694-3696 3765 3891 3962 4067 4101-4102 4232-4235 4383-4384 4461-4464 4533 4546-4548 4581-4582 4796-4797 4882 4886 4899 4907-4910 4967-4970 5073 5078 5295-5296 5431-5433
rectum	Invitrogen	REC001	39-40 61 64 278-283 298-300 491-492 561-562 652-653 789-793 870 879-881 957-960 997-998 1007 1042-1043 1070-1071 1131-1136 1159 1217-1218 1235-1242 1272-1273 1275-1277 1317-1319 1363-1371 1380 1386-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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salivary gland	Clontech	SAL001	48-50 116-119 154-156 175-177 313-315 396-398 491-492 543 591 784-786 826-828 910-914 924 950 994-995 999 1023-1025 1036-1037 1049 1128 1202-1204 1230-1232 1237-1242 1297 1322 1332-1333 1352 1418-1420 1446-1449 1473 1480-1484 1498-1499 1507 1511-1512 1533-1535 1541-1546 1667-1670 1686 1746 1763-1769 1792-1795 1839-1844 1857-1859 1865-1875 1882-1885 1919-1922 1948-1949 1951 1978-1979 2017-2020 2055-2056 2118 2125-2130 2138-2142 2146-2147 2179-2181 2251-2252 2255-2257 2273 2280 2286-2287 2395 2403 2405-2413 2423 2499 2536 2591 2629-2631 2700 2712 2781 2784 2843-2845 2855-2856 2898 2965-2968 3008 3021-3022 3075 3236 3280-3282 3319-3322 3462 3491-3495 3632-3634 3778 3867-3869 3966-3968 4291-4295 4333 4581-4582 4598-4601 4681-4683 4729 4953 5001-5003 5148-5149 5270 5272-5274 5406-5407 5464-5466
salivary gland	Clontech	SALs03	341-344 1089-1091 1435-1436 1511-1512 1664 1708 4907-4909 5272-5274
skin fibroblast	ATCC	SFB001	491-492 1089-1091 1182-1184 1685 2005 2223 5423-5425
skin fibroblast	ATCC	SFB002	175-177 1089-1091 1182-1184 1688-1689 1763-1764 3289-3290 5423-5425
skin fibroblast	ATCC	SFB003	366-367 840-844 1089-1091 1557 1688-1689 2005 3313 5423-5425
small intestine	Clontech	SIN001	154-156 179 191 201-205 212 277 341-344 357-361 435 457 652-653 698 873-875 944 969 997-999 1032-1034 1048 1063-1067

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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skeletal muscle	Clontech	SKM001	1-2 154-156 175-177 216-218 245 313-315 346-349 354 574-577 849-851 928-929 957-960 971-974 1003-1006 1032-1034 1076 1300-1301 1334-1335 1395-1396 1403-1404 1432 1550 1691-1692 1735-1739 1746 1830 2049 2118 2548 2560 2592 2629-2631 2746 2785 2819 2843 3121 3181-3183 3310-3311 3432 3663 3737-3738 3943-3948 4534 5095-5097
skeletal muscle	Clontech	SKM002	1688-1689 2234-2242 2288-2291 3795-3800 5423-5425
skeletal muscle	Clontech	SKMs03	1688-1689 3795-3800
skeletal muscle	Clontech	SKMs04	1585 3536-3543 3795-3800 5154-5157
spinal cord	Clontech	SPC001	30-31 74-77 123 134 154-156 175-177 213-215 301-303 313-315 421 491-492 520-521 751 796 822-823 849-851 855-856 863-869 871-872 889-897 909 924 927 950-953 964-966 980-988 997-998 1017-1021 1026-1027 1049 1053-1054 1089-1091 1127 1151-1154 1159 1173 1175 1182-1184 1189-1191 1215-1216 1220-1221 1230-1232 1319-1321 1349-1350 1355 1359 1363-1371 1388-1393 1398-1399 1422-1423 1432 1446-1449 1470 1532 1539 1541-1546 1551-1552 1569-1574 1582-1584 1649-1653 1663 1685 1688-1689 1707 1715-1716 1727 1735-1736 1792-1798 1831-1834 1839-1844 1915-1922 1951 1992 2005 2017-2020 2035 2042-2043 2057 2060-2061 2072-2074 2086-2087 2096-2097 2118 2143-2144 2173 2186-2187 2193-2195 2208-2210

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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adult spleen	Clontech	SPLc01	491-492 548-550 561-562 641 652-653 801- 803 863-869 944 969 971-974 995 1128 1171 1205-1207 1271 1290-1291 1330-1331 1353- 1354 1508-1510 1547-1548 1551-1552 1605- 1608 1621-1623 1625 1694-1698 1743-1745 1753 1796-1798 1827-1829 1848-1851 2054 2066-2067 2098-2100 2111-2114 2179-2181 2193-2195 2537-2538 2604 2925-2929 3017- 3020 3234 3240 3250-3252 3289-3290 3402 3536-3543 3667 3975-3983 4114-4116 4136 4549 4652-4653 4691-4692 4796-4797 4907- 4909 5001-5003 5050-5052 5144 5241-5242 5270 5335-5343 5346-5354 5389-5391
stomach	Clontech	STO001	47 134 154-156 286-287 394 440-441 468 707 754 950-953 961-962 995 1041 1050 1070-1071 1075 1160-1164 1182-1185 1195- 1196 1256 1414 1507 1511-1512 1524 1638 1648 1664 1674-1682 1687 1724 1746 1780- 1783 1819 1952-1953 2093 2118 2121-2124 2188 2216-2221 2234-2242 2251-2252 2258- 2260 2273 2424 2464 2511-2513 2522 2548 2626 2645-2647 2650 2664 2675-2676 2686 2726 2820 2842 2898 2957 3008 3114 3172- 3173 3197 3258-3259 3285 3310-3311 3374- 3382 3428-3429 3456 3508-3513 3584-3585 3693 3882-3883 3906 3969-3971 4241-4242 4400 4498-4500 4672-4674 4910 4967-4970 5431-5433 5497
thalamus	Clontech	THA002	14-22 52 70 96 131-132 154-156 235 296 313-315 354 400-404 436 551-553 709-711 822-823 829 964-966 969 997-998 1026-1027 1038-1040 1044-1047 1051 1129-1130 1154 1175 1182-1184 1193 1244-1246 1249-1255

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
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thymus	Clontech	THM001	28 39-40 42 52 125 137 157-159 165 175-177 198 235 274 277 284 366-367 394 450-451 491-492 499 516 583-590 605-606 659-660 707-711 764-771 822-823 840-844 847 852- 854 863-869 899 944 950-953 980-988 997- 999 1017-1021 1026-1027 1075-1076 1080 1131-1136 1139-1142 1173-1174 1182-1184 1202-1204 1230-1232 1290-1291 1308-1309 1359 1380 1389 1397 1410 1414 1418-1423 1434 1444 1450 1470 1479 1485 1507 1511- 1512 1516-1517 1524 1551-1557 1569-1574 1597 1611 1617-1619 1659-1660 1663 1686 1709-1714 1719-1721 1727 1746 1753 1763- 1764 1792-1795 1827-1829 1857-1859 1876- 1877 1879-1881 1915-1922 1926-1927 1954- 1962 2000-2002 2031-2034 2038 2049 2054 2060-2061 2098-2100 2118 2125-2133 2138- 2142 2145 2148-2150 2153-2160 2191-2192 2214-2215 2246-2248 2254-2257 2267-2270 2273 2280 2284 2298-2299 2301 2307 2338- 2340 2427 2456 2468 2490-2491 2536 2542 2561-2562 2604 2730 2739 2752-2758 2820 2843 2866-2867 2873-2874 2913-2917 2919- 2920 2954 2974-2975 3009 3025 3035-3036 3088 3094-3095 3117 3149 3170-3171 3210- 3211 3226-3229 3235 3238 3250-3255 3283 3289-3290 3314 3342-3344 3428-3429 3508- 3513 3591-3593 3605 3608 3624-3625 3632- 3634 3636 3689 3691 3723 3772 3778 3780- 3781 3784-3786 3815-3816 3864-3865 3882- 3883 3891 3897-3905 3925-3926 3958 3962 4093 4100 4112-4116 4126-4130 4228 4287- 4288 4581-4582 4598-4601 4652-4653 4662

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			4796-4797 4839 4910 5000-5003 5137-5140 5148-5149 5190-5192 5272-5274 5317-5320 5384 5483
thymus	Clontech	THMc02	39-40 52 74-77 92-96 136 154-159 168 175-177 244 258-260 301-303 316-320 365-367 400-404 462 471 491-492 498 516 522-524 531-532 551-553 557 602-603 607 647-649 670-671 697 699-701 709-711 728-733 784-786 822-823 829 833 840-844 863-869 885-886 925-926 931-936 944 950 971-974 993 995 997-999 1003-1006 1017-1021 1042-1047 1070-1071 1075 1110-1113 1128 1131-1136 1171 1182-1184 1192 1202-1207 1271 1275-1277 1315-1319 1322 1332-1333 1357-1359 1363-1371 1389 1398-1401 1405-1407 1432 1440-1441 1446-1449 1455-1462 1467-1469 1479 1507-1510 1524 1526 1533-1535 1540 1551-1552 1569-1574 1588-1589 1617-1619 1634-1637 1646-1647 1656 1694-1698 1701-1702 1707 1715-1716 1727 1743-1746 1754 1763-1764 1792-1795 1831-1834 1839-1844 1848-1851 1857-1860 1870-1877 1879-1881 1903-1911 1913-1918 1952-1962 1966-1974 1981-1983 2010-2013 2017-2024 2048 2052-2053 2060-2061 2072-2074 2080-2082 2086-2087 2098-2100 2131-2133 2138-2142 2148-2150 2153-2160 2178 2191-2192 2196 2208-2210 2214-2221 2230 2234-2242 2249 2286-2287 2331 2338-2340 2360 2388 2391 2464 2511-2513 2519-2520 2537-2538 2604 2645-2647 2651-2655 2657-2658 2672-2674 2677-2680 2737-2738 2741-2743 2781 2829 2846-2847 2896-2897 2901-2903 2918 2976 3009 3068 3124-3128 3138 3196 3215-3216 3220-3222 3230 3240 3250-3252 3274 3289-3290 3299 3310-3311 3331-3332 3394-3395 3403-3404 3406-3407 3459-3460 3466-3468 3535-3543 3554-3556 3591-3593 3654-3657 3729-3730 3737-3738 3768-3769 3795-3800 3817-3821 3846 3867-3872 3878-3879 3882-3883 3925-3926 3969-3971 3975-3983 4100 4106 4285-4288 4291-4296 4326 4343-4347 4360 4376-4377 4439 4529 4534 4542-4544 4581-4582 4598-4601 4613-4615 4622-4623 4629-4632 4651 4657 4660 4672-4674 4729 4747-4749 4796-4797 4864-4865 4903 4907-4909 5001-5003 5046-5047 5130-5131 5148-5149 5210 5241-5242 5261-5267 5276-5277 5298-5302 5313-5315 5322 5329-5330 5332-5333 5335-5343 5346-5354 5421-5425 5440-

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			5442
thyroid gland	Clontech	THR001	1-2 47 62 70 74-78 100-106 134 136 138-139 154-156 175-177 185 191 197 222 231 237- 240 252-253 278-283 313-315 332-333 341- 344 357-361 365 379-380 394 400-404 415- 416 419 437-438 463 491-492 511 513 574- 577 583-590 631 652-653 670-671 685 699- 701 704-707 728-733 796 822-823 840-844 847 863-870 889-898 903-908 910-914 916- 918 927-929 931-936 944 951-953 969 971- 974 980-988 992-995 997-999 1003-1006 1008-1009 1017-1021 1032-1034 1036-1037 1049 1052-1054 1056-1057 1063-1067 1070- 1071 1075 1079 1110-1113 1117-1121 1128- 1136 1154 1172-1173 1175 1180-1187 1198- 1204 1217-1218 1220-1223 1228 1235-1236 1243-1246 1249-1255 1266-1267 1269-1271 1275-1277 1286 1297 1300-1301 1307 1310- 1319 1323-1327 1332-1333 1349-1350 1353- 1355 1359-1362 1374 1386-1387 1389-1393 1395-1399 1403-1404 1412 1414-1420 1427- 1431 1438 1440-1444 1446-1449 1455-1456 1463-1464 1470 1473 1479-1480 1488 1507- 1510 1520 1524 1536-1538 1547-1548 1551- 1552 1558 1569-1574 1582-1584 1586-1589 1611-1612 1617-1620 1639-1645 1648 1657- 1658 1663-1665 1667-1670 1683-1684 1686 1691-1692 1701-1702 1707 1715-1716 1723 1735-1739 1746 1753 1755-1756 1765-1771 1773-1774 1780-1783 1792-1798 1805-1813 1827-1834 1839-1844 1848-1852 1870-1877 1897 1903-1911 1915-1918 1925-1927 1951 1954-1962 1964-1974 1999-2003 2005 2010- 2013 2017-2020 2025-2026 2036-2038 2042- 2043 2045-2048 2050-2059 2062-2064 2066- 2071 2075 2083 2086-2091 2093 2101-2102 2111-2114 2116 2118 2125-2133 2143-2144 2156-2160 2163-2168 2173-2176 2179-2181 2186-2187 2200-2210 2223 2230 2253-2260 2262 2267-2270 2273 2288-2292 2296-2297 2303-2304 2327-2331 2358 2377-2379 2386 2418 2421 2423 2427 2434-2435 2444 2449 2452-2454 2467 2496 2502 2510-2513 2534- 2536 2549-2550 2554-2556 2564-2571 2573- 2575 2598 2604 2626 2629-2631 2645-2648 2650-2655 2657-2662 2672-2676 2686 2700 2702-2706 2709-2711 2726 2741-2743 2746- 2748 2760-2761 2763 2772 2777-2778 2805- 2806 2813-2814 2818 2828 2833 2843 2852- 2853 2861-2862 2866-2867 2898-2900 2905



Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			2913 2925-2929 2945-2946 2965-2973 2992 3008 3010-3012 3021-3022 3024 3084-3085 3088 3094-3095 3123 3131 3133-3135 3138 3153-3158 3170-3171 3189-3191 3195 3210- 3212 3218 3220-3222 3226-3228 3240 3242- 3243 3256 3258-3259 3279-3282 3288 3297- 3299 3313 3319-3322 3325 3331-3335 3342- 3346 3372-3382 3399 3408 3418 3424-3429 3438-3441 3444-3445 3456 3466-3468 3474 3477-3478 3516-3517 3522 3524-3532 3535 3544-3545 3554-3556 3558-3562 3577-3580 3583 3586 3589 3591-3593 3602-3605 3610- 3613 3628 3638-3640 3658-3660 3673-3677 3680 3685 3691 3693 3708 3724-3725 3747 3762 3791-3792 3804-3807 3815-3816 3822- 3824 3867-3869 3871-3872 3886 3891 3895 3908 3930 3949-3951 3962 3966-3971 4004- 4007 4014-4015 4024-4025 4033-4034 4043- 4045 4093 4100 4104-4105 4109-4111 4123 4126 4140-4141 4169 4220-4223 4230-4235 4241-4244 4275-4277 4379-4380 4383-4385 4435-4437 4461-4464 4520 4522 4537-4544 4568 4581-4582 4598-4601 4633-4635 4640 4681-4683 4691-4692 4764-4766 4785 4796- 4797 4864-4865 4873 4890-4891 4907-4910 4980 5085-5088 5092 5107-5108 5147-5149 5154-5157 5241-5242 5280 5308-5309 5329- 5330 5335-5343 5369 5389-5391 5399-5401 5406-5407 5423-5425 5427-5429 5442 5448- 5450 5464-5466 5497
trachea	Clontech	TRC001	1-2 39-40 52 231 288-290 306 379-380 511 822-823 889-897 909 951-953 963 990-991 1026-1027 1052 1110-1113 1129-1130 1182- 1184 1272-1273 1292-1293 1297 1300-1301 1307 1349-1350 1352 1363-1371 1397 1440- 1441 1457-1462 1511-1512 1532 1547-1548 1586-1587 1612 1648 1664 1667-1670 1687 1690 1708 1735-1736 1746 1770-1771 1876- 1877 1900-1902 1948-1949 1951-1953 2000- 2002 2004 2021-2024 2036-2037 2054-2056 2060-2064 2118 2422 2452-2454 2470-2474 2511-2513 2604 2659-2662 2681-2685 2748 2879-2881 2898 2925-2929 2974-2975 3026- 3027 3170-3171 3223 3242 3260-3267 3394- 3395 3446-3449 3456 3663 3673-3677 3686- 3688 3761 3969-3971 4014-4015 4140-4141 4275-4277 4477 4554-4555 4570-4571 4664- 4665 4761-4763 4864-4865 4878-4879 4892 5241-5242 5272-5274 5438
uterus	Clontech	UTR001	116-119 137-139 278-283 313-315 379-380

Tissue origin	RNA Source	Library Name	SEQ ID NOS:
			491-492 548-550 583-590 592-594 789-793 814-816 822-823 930 995 999 1050 1068 1143 1202-1207 1230-1232 1297 1323-1327 1351 1363-1371 1383-1384 1388 1425 1438 1451-1454 1507 1551-1552 1582-1584 1627 1663 1688-1689 1691-1692 1719-1721 1746 1753 1755-1756 1765-1769 1792-1795 1839- 1844 1878 1919-1922 1951 1988 2017-2024 2045-2047 2055-2056 2118 2193-2195 2208- 2210 2254 2273 2296-2297 2444 2469 2552 2604 2665 2696-2697 2768-2771 2781 2802 2861-2862 2955 3156-3157 3419 3451-3455 3577-3580 3708 3729-3730 3749-3752 3880 3934 3966-3968 4043-4045 4062-4064 4239- 4240 4374-4375 4629-4632 4666 4796-4797 5024 5148-5149 5181-5183 5389-5391 5485

\*The 16 tissue-mRNAs and their vendor source, are as follows: 1) Normal adult brain mRNA (Invitrogen), 2) normal adult kidney mRNA (Invitrogen), 3) normal adult liver mRNA (Invitrogen), 4) normal fetal brain mRNA (Invitrogen), 5) normal fetal kidney mRNA (Invitrogen), 6) normal fetal liver mRNA (Invitrogen), 7) normal fetal skin mRNA (Invitrogen), 8) human adrenal gland mRNA (Clontech), 9) human bone marrow mRNA (Clontech), 10) human leukemia lymphablastic mRNA (Clontech), 11) human thymus mRNA (Clontech), 12) human lymph node mRNA (Clontech), 13) human spinal cord mRNA (Clontech), 14) human thyroid mRNA (Clontech), 15) human esophagus mRNA (BioChain), 16) human conceptional umbilical cord mRNA (BioChain).

Table 2

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
1	5498	C	1	239	322	MGGALLKEPILSPGGGKGKIFFWGPQN*
2	5499	A	2	1441	2129	SVIA*SCRASVASKQS*PTLLPSACARPHA\STVDAPASGGAPRASSP\SSDCLWSTSSSSTPLSASASSS/SPPSFNP AADARGSQGPARGRSCSPSSSERH VRRRVSAARQAGAASAGGGRQAGLAGRSGLSA/SRSSARASSSATPALAQST\PSSSESECAPLKSRSGLTSSL SKP AS*ATLGKKGSGSSWRFPPESI HGR HPLSASCWNKSVAAAAAPTGATAP PKAGP
3	5500	C	3	36	236	MGPTIPDXSXXFFWRKPITWMPTWEGTSNVGPQPLSSSKSLHSXRGHPAPIPTGQAGPRDSGPGASP*
4	5501	A	4	109	300	GGGKQIPFKGGKFKWGPV LKKG EREKPGGNPKKTPWKKASSRPAPRI HPCFT*HAPDPRPLY
5	5502	A	5	2	73	
6	5503	A	6	27	375	EHSQVRQALCFGTASQRP SQPAPS GPGPPGEPG*ERLCASHKAFISHKQS H*SPQ*PCQAGVTL SRLQT TNSPRPH SQKGLRGPRQTQLSLTSQPTACSEN SQGSQSPKRTLS
7	5504	B	7	50	204	XKEGSLCDEYWNPAANLINVCSLFLRQGPRLALMQGEPVDKGCLGV LLE NK*
8	5505	A	8	379	623	ATTVSVPFPTAKLLERPGLHLLVFLPNLQFPLQPLVS*LALLRGSTLTKQVPSAPDKPLLVSPPAKHPPVPPSCGPG LQG
9	5506	B	9	185	366	XHPGDGFRPNQEGDERPARKKTWVRDGGPHQGLFRSFHPQFFSRPSRATAHVPVYFSVEWX*
10	5507	A	10	29	308	WLPPNPGRRRREARQEEDLPGPWWAPSGPLPQLPSAVLQPTQPGHGPRASL**SVCFSFADKEGSLCDEYWNPA A/KPH*RLQPLPSTRPEISPL
11	5508	A	11	663	1269	TAGTWAVASLGR LKNCGWKL RKEALMGPTIPDPKSSPLAGLSSFPWFGRKPITLECPTWERDPRNVGPPAPSPARKSLPQPTGTTLPYSPRDKAGPK KTLGPRG/APL*VRRTRPLN*WTPA DLGVRTRGAGPLPDAGTLRPRGAVEPSVSACGKWAPSPTSQGCCEGR CDAVPKHEGLAHPTVLSINVFPVLN QKKKKK
12	5509	A	12	190	715	
13	5510	A	13	270	713	KLTLDCQFTG*QR*KFNG*NLRNR/HSPSRWDGAKPLYKALKL*SSSSSV GAFIFIFTRSLRAYLFSFAH/LRRPL LAGHLLCSPEQAVELSALLAQTKFG DYNQNTAKYNYEELCAKELSSATL

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
14	5511	A	14	1575	1968	NSIVAKHKELEGTSQASAEYQVL REMGFRHVGQTGLELLTSGDLPTSA SQSAGITGVSHHTWPKTLFVLRQSL TLSPGLECSGTISAHCSPHLPCSSNS CAPASRVAESTEAAHH/LCPDNLHISS REGASPCWPGCS*TPELKRPAHPCR DQLGH
15	5512	A	15	185	720	KVSHVYFLHRHGNHPISQTFPHLS PLSIPQNCHCHGPFMSWCWRIKYL GIQLTRDVKDLFKEN*KPLLSKIKED TNKWKNIPCSWIGRINIVKMAILP/K ELEKTTLKFIWNQKRACIAKTILSQ KNKAGDITLPDFKLYKATVTKTA WE\QNRDIDQWNRIEPISEITPHIYNY LIF
16	5513	A	16	1114	2193	GSFTKRVRRAFKVLRDNPVAKLS QVKKHWHYFTWNHKKRLKIAKAILSK KNKPGGITLPDFKL*YRATVSKTVW YWHKNRHINQWNRIRNPEANAHTY I*LIFDKGAKNIHWVKTSLFNKWCW EN*ISIC\KEWEKISANYPSPDKGLITR IYKEL/K/QL*EKKSNNLIKQAKDL NRHFSKEDK*MANRHMKKCSMLIT REMQIKTTMKYHFTPVKMYIQKA GNDKCWQGCGEKGTFFVHC*WECK LV*PL*RTVWRFLEKL/E/LELP*DPA IPLLGIYPK*RKS/CVIKEITVAKIWK QPKCPSTDKWIKKMWYIYTMDYYS ALKKNEILSFPTTWELKIVILSVIG QSQKDKHCMFSLICGS
17	5514	A	17	149	328	WQDPLQDPCCHQPFHLCLRR*TLH* LRQQ*WPLLRLRGKIMLILLNTHP EHPCVLLDL
18	5515	A	18	615	734	ENSCWTATLQMGKNWQSL*PVLTS YYR*DNSYWREILQV
19	5516	A	19	1	181	MRARRLPWALTVAELGWDTOGG DQTSPPGGNDRMSMEAECSTTVSP LSCSIPTGCGQTREEVSARATPPPSL GASLLQTLTPDTHCTGVSA*KLATF FTFVGFLLSSMNCLMLSKG*GTAKSF ATFTTFVGLLSSVYPLMSS
20	5517	A	20	1	665	
21	5518	A	21	401	1739	DNSHWRETLMQ*RMWQSF*PFFNP C*T*ENSYW/MRNPTNVKNVAKLL AIPQPLLIIR*LILKRNPNTNVKNVTKL LSDSQPLLNK*YMLERNSTNVKNV AKLLIDLQILLYISLFILERNLTSVKN VAKHLTGPQALLNIKDFILERNPSN VKNVAKHLYGLQP*LDIRGYTLER NPTNVKNVAKLLAILQPLLNIREFIL ERNPTNVKNVAKLLAVLQPLLNIRE FILERNPTNVKNVAKLLAIPQPLLIIR
22	5519	A	22	618	1655	DIPERNASNVKNVSSHFAVYTKTQ HKCVYITEKSCCKCECEKTFHWSST LTNHKEIHTEKPYKCEECGKAFKQ LSTLTTHKIIKAKEKIYKCEECGKAF LWSSTLTRHKRIHTGEKPYKCEECG

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						KAFSHSSTLAKHKRIHTGEKPYKCE ECGKAFSHSSALAKHKRIHTGEKPY KCKEKGKAFSNSSTLANHKITHTEE KPYKCKECDKTFKRLSTLTKHKIIH AGEKLYKCEECGKAFNRSSNLTIHK FIHTGEKPYKCEECGKAFNWSSSLT KHKRFHTREKPFKCKEKGKFIWSS TLTRHKRIHTGEKPYKCEECGKA QSSLTTKHKIIHTGEKPYKFEECGK AFRQSLTLNKHKIIHSREKPYKCKE CGKAFKQFSTLTTHKIIHAGKLYK CEECGKAFNHSSSLSTHKIIHTGEKS YKCEECGKAFLWSSTLRRHKRIHTG EKPYKCEECGKAFSHSSALAKHKRI HTGEKPYKCKEKGKAFSNSSTLAN HKITHTEEKPYKCKECDKTFKRLST LTKHKIIHAGEKLYKCEECGKAFNR SSNLTIHKFIHTGEKPYKCEECGKAF NWSSSLTKHKRIHTREKPFKCKEKG KAFIWSSTLTRHKRIHTGEKPYKCE ECGKAFSRSTLTKHKTIHTGEKPY KCKEKGKAFKHSSALAKHKIIHAGE KLYKCEECGKAFNQSSNLTTHKIIH TKEKPSKSECDKAFIWSSTLTEHK RIHTREKPYKCEECGKAQSQPSHLT THKRMHTGEKPYKCEECGK/RP*PI LNPYYT*DNSYWRETLQM*RMWQ SF*EIFNSY*T*DNSYWRETLQM*R MWQSI*PILNPN*TYEDAHWRETIQ M*RMWESF*SILKAYYT*DNSYWR ETLQI
23	5520	A	23	1	3476	MTLNEHAAFKHLFNKAHLAPPLIHL TLSGHSTCFREHRVGAKSNNPPASK GVWALQSARVKFAETTAGQKGMN TTWVFYYPNVASTWWGAMIPVHV VLPGGCHDASTLGDKEKRAGEAVL NVPGFQDSLESHGRIVNCLIPDVQE NNPSTGNESWLKSHQRLGEPTSRR WLITLPVTSRSNSIGHLKGTGPKSKE EIKATVCAPTLKNGFWIAERVMTVS GHEGAASSRALREELRLLFSSCAQG RLTPHIAGYPSKAKLREERSGSNICC SAIFAVLQPLLLIPRGTGSGVDLLQT PTDLQLRVLTVRRKTNKQEGHPHQ NPTCTSPSSKTKDRSTRNVKQDTQ ELNSALRQVDLIDYRTLHPKSREYT FFSAPHRTYSKIDHTVGSKALLSKR KRTEIITNCLSHHSAIKLELRICKLTQ NRSTTWKLNLLNDYWVHNEMK AEIKIFFETNENKDTTYQNLWDTFK AVCRGKFIALNAHKRKQERSKIDTL TSQLELEKQEQTHSKASRRQEITKI RAELKEIETQKNLQKINEFRS/W/PW QRHNKKK\KFWTNTPDHQCCKNPQ *NTGKPNPAAHQKGYPP*SSGLHPW DARLVQHTKINKRNPSYKQNRQK PHDYLNRCRKGL*QNSTALHAKNS Q*IRY*WDVSQNNKSYL*QTHSQYH

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						SECAETGSIPFENWHKTGMPSLTTP QHSGVSSGQGNHAGERKNGYSIRK RGSQIVPVCR*HDCAFRKPYGLSPK SP*ADKQLQQSLRIQNQCTKTTSILI HQ*QTNREPNE*TSIHNCFKENKIL RNPTYKGCEGPLQGELQTTAQ*NK RGYKQMEEHSMMLMGRRI SYHENG HIAQGNLQIQCHPHQATNDFLHRTG KNYFKVHMEPKKSPHHQGNPKPKA QSWRHHTT*LQTLQGYSNQNSMV LVPKQRYRSMEQNRALRN NATYLQ LSDL*QT*EKQAMGKGFP**TVLG KLASHM*KAETGSLPYTLYKN*FK MD*RLKR*T*NHKNPRRKPRHYHS GHRHGQGLHV*NTKSNGNKSQNG QMGSN*TKELLHSKRNYHQSEQAT YKMGENFRNLLI*QRANIQLQRTQ TNLQEKNKQPYQKV GKGHEQTLLK RRHLCSQKTHEKMLIITGHQRNAN QNHNEIPSHTN*NGNH*KVRKQQG HG
24	5521	B	24	1	8442	MIPARFAGVLLALALILPGTLCAEG TRGRSSTARCSLFGSDFVNTFDGSM YSFAGYCSYLLAGGCQKRSFSIIGDF QNGKRVSLSVYLGEFFDIHLFVNGT VTQGDQRVSMPLYASKGLYLETEAG YYKLSGEAYGFVARIDGSGNFQVL LSDRYFNKTCGLCGNFNIFAEDDFM TQEGTLTSDPYDFANSWALSSGEQ WCERASPPSSSCNISSGEMQKGLWE QCQLLKSTSVFARCHPLVDPEPFVA LCEKTLCECAGGLECACPALLEYAR TCAQEGMVLYGWDHSA CSPVCPA GMEYRQCVSPCARTCQSLHINEMC QERCVDGCSCPEGQLLDEGLCVEST ECPCVHSGKRYPPGTSLSRDCNTCI CRNSQWICSNEECPECLVTGQSHF KSF DNRYFTFSGICQYLLARDCQDH SFSIVIETVQCADDRDAVCTRSVTV RLPGLHNSLVKLKHGAGVAMDGO DVQLPLLKGDRLRIQRTVTASVRLSY GEDLQMDWDGRGRLLVKLSPVYA GKTCGLCGNYNGNQDDFLTPSGL AEPRVEDFGNAWKLHGDCQDLQK QHSDPCALNPRMTRFSEEACAVLTS PTFEACHRAVSPLPYLRNCRYDVCS CSDGRECLCGALASYAAACAGRGV RVAWREPGRCELNCPKGQVYLQCG TPCNLTCSRSLSPDEECNEACLEG FCPPGLYMDERGDCVPKACQPCYY DGEIFQPEDIFSDHHTMCYCEDGFM HCTMSGVPGSLLPDAVLSSPLSHRS KRSLSRPPMVKLVC PADNLRAEG LECTKTCQNYDLECM SMGCVSGCL CPPGMVRHENRCVALERCPCFHQG KEYAPGETVKIGCNTCVCRDRKWN CTDHVCDATCSTIGMAHYLTFDGL KYLFPGECCQYVLVQDYCGSNPGTF

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						RILVGNKGCSHPSVKCKKRVTILVE GGEIELFDGEVNVKRPMDETHFE VVESGRYIILLGKALSVVWDRHLS ISVVLKQTYQEKVCGLCGNFDGIQN NDLTSSNLQVEEDPVDFGKSWEVSS QCADTRKVPLDSSPATCHNNIMKQ TMVDSSCRILTSDFVQDCNKLVDPE PYLDVCIYDTCSCESIGDCACFCDTI AAIAHVCAQHGVVTVWRTATLCP QSCEERNLRENGYECEWRYNSCAP ACQVTCQHPEPLACPVQCVEGCHA HCPPGKILDELLQTCVDPEDCPVCE VAGRRFASGKKVTLNPSDPEHCQIC HCDVVNLTCACQEPGGLVVPPTD APVSPTTLYVEDISEPPLHDFYCSRL LDLVFLLDGSSRLSEAEFEVLKAFV VDMMERLRISQKWVRVAVVEYHD GSHAYIGLKDRKRPSELRRIASQVK YAGSQVASTSEVLKYTLFQIFSKIDR PEASRIALLMASQEPQRMSRNFVR YVQGLKKKKVIVIPVGIGPHANLKQ IRLIEKQAPENKAFVLSSVDELEQQR DEIVSYLCDLAPEAPPPTLPPDMAQ VTVGPGLLGVSTLGPKRNSMVLVDV AFVLEGSDKIGEADFNRSKEFMEEV IQRMDVGQDSIHVTVLQYSYMVTV EYPFSEAQSKGDILQVRVREIRYQGG NRTNTGLALRYLSDHSFLVSQGDRE QAPNLVYMTGNPASDEIKRLPGDI QVVPVIGVGNANVQELERIGWPNAP ILIQDFETLPREAPDLVLQRCCSGEG LQIPTLSPAPDCSQPLDVILLDDGSSS FPASYFDEMKSFAKAFISKANIGPRL TQVSVLQYGSITTIDVPWNVVEKA HLLSLVDVMQREGGPSQIGDALGF AVRYLTSEMHGARGASKAVVILV TDVSVDSVDAAADAARSNRVTVP IGIGDRYDAAQLRILAGPAGDSNVV KLQRIEDLPTMVTLGNSFLHKLCSG FVRICMDEEDGNEKRPGDVWTLPDQ CHTVTCQPDGQTLLKSHRVNCDRG LRPSCPNSQSPVKVEETCGCRWTC CVCTGSSTRHIVTFDGGQNFKLTGSC SYVLFQNKQDLEVLHNGACSPGA RQGC MKSIEVKHSALSVELHSDME VTVNGRLVSVPYVGGNMEVNVYG AIMHEVRFNHLGHIFTFTPNNEFQ LQLSPKTFASKTYGLCGICDENGAN DFMLRDGTVTDDWKTLLVQEWTVQ RPGQTCQPILEEQLVPDSSHQVQL LLPLFAECHKVLAPATFYAICQQDS SHQEQVCEVIASIAHLCRTNGVCV DWRTPDFCAMSPPSLVYNHCEHG CPRHCDGNVSSCGDHPSEGCFPPD KVMLEGSCVPPEACTQCIGEDGVQ HQFLEAWVPDHQPCQICTCLSGRK VNCTTQPCPTAKAPTCGLCEVARLR QNADQCCPEYENGRLVSVPYVGGN

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						MEVNVYGAIMHEVRFNHLGHIFTF TPQNNEFQLQLSPKTFASKTYGLCG ICDENGANDFMLRDGTVTDDWKT VQEWTVQRPGQTCQPILEEQCLVPD SSHCQVLLLPLFAECKVLPATFY AICQQDSSHQEQVCEVIASIAHLR TNGVCVDWRTPDFCAMSPPSLVY NHCEHGCPRHCDGNVSSCGDHPSE GCFCPPDKVMLEGSCVP EEACTQCI GEDGVQHQFLEAWVPDHPQCQICT CLSGRKVNCTTQPCPTAKAPTCGLC EVARLRQNADQCCPEYENPCPLGY KEENNTGECCGRCLPTACTIQLRGG QIMTLKRDETLQDGDTHFCKVNE RGEYFWEKRVTCPPFDEHKCLAE GGKIMKIPGTCCDTC EEPESNDITAR LQYVKVGSCCKSEVEVDIHYCQGKC ASKAMYSIDINDVQDQSCCSPTRT EPMQVALHCTNGSVVYHQVLNAM ECKCSPRKSSK*
25	5522	A	25	364	477	VIEHLVSQDGLDFLTS*SARLGLPKC WDYRREPPRPVH
26	5523	A	26	6838	7166	GSRRPGCHCNSHTGRRSSRHRGHL SPAASRGHPSPSAGPPRS*GARRPSL YAGYEAYLSGGGAGRPGHPWQLLP HASVSQGCCAGQAAGR*RSGCTQR RGQSSPGQSQ
27	5524	A	27	817	1299	RKSHIFFFFLRWSLALSPRLECSGA ILAHCKLLLP/GFKPFSCLSQPSSWD YRHPPRPANFLYF/SVETGFHHVSQ G\GLNLLTS*SAHLSLPKCWDYRRE PPRPAENLSSLTQYLECTQFEIHLGS QTALEGRLVPVTPYPLGGVEISGHPV FLLTSSCGR
28	5525	A	28	506	761	DGVLLLLPRLECNSAILAHRNLRPL/ GFKRFSCLTLLSPWDYRHLPPRLAIF FVFLVYVGFHHVGYAGLE\LLTSR* SARPRPPKIA
29	5526	A	29	71	425	CRRKGVNMNAPLGGIWLWLPLLLT WLTPEVNSSWRYMIATGGSCRVMC YNELGLVSRRLCQRYSPCILTLY GEAKVLFVCGLSLLVHWPN\CAPSF RDNT*LLRFLHVIIVLLRPL
30	5527	A	30	263	463	
31	5528	A	31	287	2919	MASFPPRVNEKEIVRLRTIGELLAP AAPFDKKCG\RENWTVLAPDGSY FAWSQGHRTVKLV\WSQCLQ\NFL \LHGTKNVTNFKQFKDLPRQNS\DG GSEKIKPREHIIDCGDIVWSLAFGSS VPEKQSRCVNIEWHRFRFGDQQLL ATGLNNGRIKIWDVYTGKLLNLV DHTGVVRDLTFAPDGSLLVSASRD KTLRVWDLRDDGNMMKVLRGHQ NWVYSCAFSPDSSMLCSVGASKAV VAAILV*LRLCWHHSHTGAQWC*L GRKSGISGYRAGGDLYHRMK*PCIR LQGVLYVHRCWSMSTFCFFLFF FKVISPTVKYTDS*VN*FSSFME LGV



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						*QVKPI*CKVFGFQMVSLCYFLEFF QIPEISYVFDSI*NL YLFSFRNNVLCL CRKKKNQKGLLYSKRRDCLRLNLO AHI*YNRLK*TLESCLELFCVTNY*S LESKIVYELILK*LNCFIFK*LMIVVS LGKIRWLNFDLLKCNCIIFIK*HFHF VMWFNILVVCQRNFIWL*IFYLLAV SVSLPRLKLVTQAYCKQVIISKGDA NGVTIC*PYVFCLYIF*KSGSFWKKK EKGVCST*PYLFPYILVN*FLE*MDF SIALWLNCFILCLGLFLN*HLTETF EIEFACLP*LT*RLILI*L*H*AYSLNY S*FIMLNILIKFSSFSIRCAILSSVCLN EAITFAFLQVFLWNMDKYTMMRK LEGHHHDVVACDFSPDGALLATAS YDT*VYIWDPHNGDILMEFGHLFPP PTPIFAGGANDRWVRSVSFSDGLH VASLADDKM\VRFWRIDEDYPVQV APVSNGLCACAFSTDGSLAAGTHD GSVYFWATPRQVPSLQHLCRMSIRR VMPTQEVQELPIPSKLEFLSYRI
32	5529	B	32	51	285	XGDEKGAAQVAAVLAQHRVALSV QLQEACFPFGPIRLQVTLEDAASAA SAASSAHVALQVFSELGFPPAVQR WVIGRCL*
33	5530	A	33	38	347	FGVAPGVSLHHPRPHPARATASTR RAWNPQALPQPSGSSAVGSPSPRC HRGRTEW\QCPVMDTITIWNSLGPP VLVGEVGSTFPTAGCLGRLPGGSR WSLE
34	5531	A	34	331	1257	FRGCHRGKDRMAARVTHHQPAWQ KHALASWSPPEASTLKGPPEADL PRSPGNLTEREELAGSLARAIAGD EKGAQAQVAAVLAQHRVALSFQLQE ACFPFGP\IRLQVTLEDAALPHPPAS SAHVALQVHPHCTVAAPGSRFFSE LGFP\PAVQRWFIGRCLCVPERSLAS YGVR\RDGDHAFLLYLLSA/RSRS/LQ PQDLALKNPQEDGRGTWTLVSPHIG GYPQGPTAQLPPACPSPLPA\SWSCP FRHLHSMPPQKRPCEMCSTQRPC WDPLAAAST*QPPEVTRGEWPFPH KSDISRPLNSGDLY
35	5532	A	35	616	1017	LYWEKIIFSNLKTPTETFLVMTSNIF HIFWEGNKLPHYTTQFSGFYFILWY FR\DRASL\CRPVWGAVVWS*LTAA SNSW\VRCSCLGLPSSWSLSPMPPH SANFKFY*FHLIFVGDGGLAVLFR VLNSWPQAI
36	5533	A	36	3	283	FYTQNIIFYSVESKLHTSTL*D\HYFFF FFETESYSIAQGGVQWGNLGSQPP SPGFKQLSCLSLPSSWNYRCAPPCP ANFVFLVEMGFHWIKPG
37	5534	A	37	260	569	RENLDLGEAFISRCLPLHSLAYFLH NLSFKSREMHNMFVKS*QALKFIRR IENNHLFFYFYFYFERKSLHSPG NGVGLCLKKKKNNNGSYKVLVWSF DSTE

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38	5535	A	38	468	849	TSEEFQQFTIHLTGVLHCHPDLETG GYKTF*WKSLEN*IAFFFFSETESPS AP\RLCSGSISAHCNLLPGSSDSPAP ASRIAGTTGTHHHARPIFILLVKEGF HHVGQPGLKLLTSGDPPAPASQSA
39	5536	A	39	97	448	GSHEQPWEVVTGSRQPAR*SSR*AI MRKPRAAVGSGHRKQAASQEGRQ KHAKNNSQAKPSACD/GDVAEVTA FRGSLLSWYDQEKRDLPWRRRAED EMDLDRRAYA\KWPTLQDLASASL EEVNQLWAGLGYYSRGRRLQEGA RK
40	5537	A	40	990	1812	RLPLGRRSPSEAAGAETAPSSLSAA MTPLVSRLSRLWVRWTC\AIMRKPR AAVSGSGHRKQAASQEGRQKHAKN NSQAKPSACDGRR*DGPGQAGICW SVHLLRA/EATLPRGPVWVGLWAR *GQVNSVL/DANPFPPVWVSKVML QQTQVATVINYYTGWMPVTPGEEG KGHGSDPR*EPLLWGGCREGFLYH LHP*PCLFLPAWGYRSGPTLQDLGR AFLEEGDQL\WAGLGYYSRGRRMP EDTPARNGTAQRSLPQHIRPLNEWP LEWRLDACREP
41	5538	A	41	360	652	IYLAGAQWLTSVILVLWKPRRVDH LRSGVRDQPGQHGETSSLLKIQKLA RRHGACL*SQLLGRWRQENHSNPG DRGCSELRL\CTPAWATEGDSVLKKK
42	5539	A	42	1400	1823	NEKKS VFLRQSL/DSVAQAGVQWC DLGSLQTPPPRFTPFSCSLPSSWDH RCPPPRPP/RFCFFLYF**RQDFTMLA RLVSNS*LQ/CDPPTLASKSAGITGM SYCTRPNQAGVQWWDLGSLQAPPP RFTPFSCSLPSSWDYRH
43	5540	A	43	227	481	KKKKELEKGNMD*IQSSRR\ETIKM RAKIF*TTNTKLMKKNKTRSLVSEN FNKIGKALARLRKKEKTPITKVRNE TEDITTNFIE
44	5541	A	44	1374	1835	ILPCNKPPWNSMACTTKHLSRSQAY RSAGAFIHWTEAGVGSALLSLAL QKPWANQGIFPCGGRSQRGVSRN TRVWVQARNWY*VTPTHRVLWMR TAPRPALAASSAASPSAVGSPVAA\ PSQPGLMTQMATTATEVVVGYAV GHTLSYSENI
45	5542	A	45	1	1470	
46	5543	A	46	62	526	EEKLKKGKSFQEYSGSLLLSIASVGF LSPTDIAIAVPRQWEEMRPLDIV*LA EPEEVEVLEPEEDFEQFLPVINEMR EDIVSLTREHG\RAYLRNRSKLLWRL DNMLI\QIKTQVEASEESALNHPPNP GET\AEG\RAAKRCEKAEEKARELQ KAK
47	5544	A	47	721	1030	MGPWEPRPQMRT*CLLPLKPNSPPP TPSEE/PGHLPK*PLEVI*WPSPPSPGF P/PAFRGQ*ARGHPPPPQWNTPFSP PQQ\PLSAGKT*PLTPFPALPYLGTG

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						RK
48	5545	A	48	66	386	PMEIFVDDEANLTLHGVQQYYLKL KDNEKNRKLFDLLDVLEFNQGVIFV KSVQRCIALAQLLVEQNFPAAIAHR GMPQEE/QFKDFQRRILVATNLFGR GMDIERVNI
49	5546	A	49	434	858	CLSHTMDPYSPNLRPPTPPHNRWVI FVKSVQRCIALAQLTSGSRNFPAIAI HRGDGPREGGGFFRVFRQF*RFENG RIFVGYQPILGRGMGHSRRVNIAFN YGHAWRVFDTYLAFGVGQRQGRF WATKGFGLFTFCVPMED
50	5547	A	50	1	660	LALARNKSLNLKHIKHFILDECCKM LEQLDMRRDVQEIFRMTPEHKQVM MFSATLSKEIRPVCCKFMQDPMEIF VDEETKLTLLHGLQQ\YYVKLKDNE KNRKLFDLLDVLEFNQVVIFLKSVQ RCIALAQLL\VEQNFPAAIAHRG\MP Q\EERLSSVFSSFKDFQRRILVATNL FGRGMDI\ERVNIAFN\YDM\EDF\D TYLHRVARAGRFGTKGLAITFVS
51	5548	A	51	143	387	QPCLTRY*DTRCTNQ*ETTS*RLCKE PFRPGSFRPNWHLANVVENIERLQL VS\TLRLIEEDSSLN*YSIIHFHSESYR YN
52	5549	A	52	2	1360	VCVCVCVCVCVRQSLAPLRLEGS VSILTHCNRLRLGLSDSPASARGA GTTGMCHHTWLMFLFLVETGFRHV GQAGLELQTS\DPALPFPKCWDYR\ VNHHARP*HSFYRSLGDQNVMA GQRPASMPCPVFLVQMSPAAVSTS VREWAPDSQRGHRDGHAKLWGVA DSPAPACPCTFGVTHETGWGSHLPS PKRQS/CYKGSQRPTQPQVIKQAPSS MATIPIHQGDVEGGASWFTPPSAET DPRSGPRTLCREGKCR*LSPYSSIKP GLKMG*IRDFHSTKEKF*WGQNIDL LIFESLLTRRERANDFVVEGPTQL*L V*SIMNANLNSRKAELPNNGTSTA MGSASSFSVCLFYERETPRKAAAH* ENVWELTRRFFIFFEMEFC\VAQA GAQWCHLGLSLQPAHHEFK*FSSA/S LPSGCDYRHPPPCPANFFYF*RDGV PSRCPGWPR
53	5550	A	53	218	380	RKMKNSSYPAPFAPRPIYSSPPPPQE/P Q*GGRDMAAIW*GALSIPPPVPDLL PLG
54	5551	A	54	76	376	YKIIFVLETCMYKVICRFANNTMHL SYTVIHKDPGKGRGIISPNLFYFIYFE MEF/SLLMPRLECNGT\AILAHRNLH LPGSSNSPASAS*VAEITGMCTMP
55	5552	A	55	97	437	WTRTHRASTCHVAYQEDGLLHLRN TNDPENFPKSYHYHRIIIGGASG*QA TAREATHYDGDVIDLDFVTPPLG TTWGLEGTCENGDSLPAIDLMHQSP LVGQPTEDFRNTGGH
56	5553	A	56	22	424	ALGMAHITLFFFFLLLFCDLALSPR

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						LQCSGTISAHCNLPVPGFKQFSCSL LGSWDYRCMPPC/RWLTFFVFLVET GFHHVGGAGLELLTSGDPPALA/FP KC*DYRR\DPRAWALFVFLT*FFSKL KYHKAKEKWS
57	5554	A	57	514	835	QFIFNVNKINSKTIKDRWGPPTVGF TPVIPQHFGRPQQANHLRSGVDR\H PGQQGETPSLLKIQK*AGHGRGHL* TQLRLRLRQENHLNLGGGGCSEPRS RHCTPAW
58	5555	A	58	234	457	SKTENIKYWLVHGELETALHRWRN SKMAY*LGK\QFLINLRTQLPYDSAI PFIGCIPFKYECWTYNKDLFTHVYI
59	5556	A	59	1	336	
60	5557	A	60	192	432	FDFNLNSPTWAGHGGSC*SQHFGR LRRVDHLRSGI*DQPG*HSKTPFL/ KNTKISWAWWRTSEIPAAREAEAG ELLELG
61	5558	A	61	81	439	CEHHKAHPPPVSPYQSMAPSFTQRL RPKEQVSPTMPFSLVSTPIHLTSGTP AGLPASIPGPLQSPWPSTTTGTAPDKI QGSPARPAQNSPVASS*ATSSPWP ARPPWTPLHSSLPALAA
62	5559	A	62	297	561	SQHFGRPRQVDHLQSGVQDH\PVQ RGETPSLLKIQKLARGGGARL*SQL LRLRLRQENHLNPGGGGCN\EPI*HR CSPA WAI*DSVSKK
63	5560	A	63	3	808	FFFWEPEKAFIEEFEGVSSSSSPSQL GQQRKQDAGVLHSWNSALKNLNV PPPPPGGWCLWGTAALSSSQAGRG SGIGRGGGESGGTG/ASSAEGEAPG GIVSCA*GPGCRSSGAKGLRLRAS SLQAPAAALIQAAPGVR*TGLGPYL SAVHAGPAAAAAALPGCLS\SPASP AAPVGATPRA\GPLNSENHRCPPGP PGPQFGLGPLGPGPGSGPWA\AHSQ NMRAAESAAAAWLSVPSQSPRLSP SSSSSSSPTAWNFSPPRDMAGLR
64	5561	A	64	1005	1150	AWAWVCVSSGLGAPCGDGCCRGR GVASKCC\CAGGGCVSVG*GNVCA RA
65	5562	A	65	3	230	LVEMGFHQPGQHGETPSLQKI*NKK \LAGHGGTCL*S*LLRRLSQEDGLSL GGRGFSEPLCHCTPA*TTEQGLKK
66	5563	A	66	317	503	KKPKPPKPPWEPTTFG/TPAFIPPRGI WFLIAPCGWV*EEGGPSGGPWPWC PLGKTHGEGGKP
67	5564	A	67	523	741	ERGFFFGPHPGGRGKKLG*WGPPFP GLKEFSPLRPP*EGGLRGPPPLPG/SF LGFLRKGGFKHGGQGGQNPGGG
68	5565	A	68	498	778	VTINMMTGIVPYISILMLNVNGLSA/ PLERRRLAEWIKIHKPNICCLQEIHL THKDSYRLNVKEWKKIFHTNGNSK *AGVAIVMSEKTDFAKATTV
69	5566	A	69	187	488	KRFGKNGFYPCGPGGLKPRALKEPP PLTPQRGGITSSSPPPQPKTLFFGY WPKKSL*INPQGGLNPSQGGKPWVG

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						GFPFLDNYGGCWNRP PGGPWGGYLK
70	5567	A	71	1006	1979	GLGASILDSTTSTWSWNASRL LIGL KNSLFFFEME/FSLLLPRLECSGTISA QV\NLRLPCSSDSSASASRVAGITGM CHHAQLIFVFLVEKGFHHVQGAGL ELTASGD/PTCLGLPKCWDYR/R*AT APGLFFFLLRQSFTLVAQAGVQWR DLGSLQPPPPPRFKQFSCSLPSTWAS WVYRHAPPCPANFVFFFFFFFFFLVE KGF\SM LRLVLNS*PHDPDPASAS QSAGITGVSHHTRPMSFKNIY\FFFF FFETESRS\VAQAGVQWRDLSSRQP PPPGFKRFSCSLSSSWDYRRVP/PM PG*FCIFRRDGVSPRWSGWSQTPDL K
71	5568	C	72	126	472	MADCCAKQEPERNECFLQHKDDNP NLPRLVRPEVDVMCTAFHDNEETF LKKYLYEIAARRHPYFYAPELLFFAK SSMNFGMKGRLRLPNRDSSVPVSK NLEKELSKHVARLSQRFP*
72	5569	A	73	3	873	HELLSTPLAFGTMKGVTL\ISLLFLFS SAYSRGVFRRDAH KSEVAHRFKDL GEENFKALVLI AFAQYLQQCPFEDH VKLVNEVTEFAKTCVADESAENC D KSLHTLFGDKLCTVATLRETYGEIA \DCC\ENKEPERNES/CFCNHHKKNP N/LPPIG*GPEVGC GCGTGFFMDNG RRTFLEKILIMEIGQEGHPYFLWPRE LLFLLLKRVLKLLFTGMLAKLAGL KLACLLAKARWDFRNEGKASSAKQ RLQCASLQKFGERAFKAWAVTRLS QRFPKAEFAEV\SKLVTDLT K
73	5570	A	74	849	1277	YNTTKLVPLYLCKMIFLLFCYVYVL RQCLA/SVAQAGMQWHNHSSLSK* PP\GLK*SSHLSLPSSWDYRCVPQRF SLLFIFCRRKGFFPILA*AGLEQLGSR NHLALASHLSVGIIGVSYHTQPVL T AAIAMVLYFVNKLSVLL
74	5571	B	75	120	323	ITRRYAEFSSALVSINQTI PNERTMQ LLGQLQVEVENFVLRVAAEFSSRKE QLVFLINNYDMMLGVLM*
75	5572	A	76	154	432	QLPEAGGPGLQEPLQLGELDITSDEF ILDEV DVHIQANLEDEL VKEALKTG VDL*LHSGERTRRD*QLPEAGGPGL QEPLQLGELDITSDEFILDEV DVHIQ ANLEDEL VKEALKTGVDLRHYSKQ VELELQQIEQKSIRDYIQESENIASL HSQITAC
76	5573	A	77	2	630	FFFVSGPAAHDLFHAVMGR TLSMT LKHLDSYLADCYDAIAVFLCIHIVL RFRNIAAKRDVPALD/RVTEFWSLM PNRPRTLLVLHDSALTDSY*PGIIN LYSHSFAPEAVVLLFDS PFSNHCPT PTTSY*PLN*MMPHSLPSPSNIPCWL TSDSD*AHRYWEQVLALLWPRFELI LEMNVQSVRSTDPQRLGGLDTRPH YVREGKGNGK

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77	5574	A	78	175	2385	QLPEVRLRGMAAAATMAAAAREL VLRAGTSDMEEEEGPAGG\GPGLQE PL\QLGELDITS\DEFILDE\VDVHI\Q ANLEDELVKEALK\TGVDLRHYSK QVELELQQIEQKSIRDYIQESENIA LHNQITACDAVLERMEQMLGAFQS *PSGSIKL\CRFRTLQE QSGAMNIRL RNRQAVRGKLGELVDGLVVP SALV TAILEAPVTEPRFLEQLQELDAKAA AVREQEARGTAACADV RGVLDRLR VKA VTKIREFILQKIYSFRKPMTNY QIPQTALLKYRFFYQFLLGNERATA KEIRDEYVETLSKIYLSYYSYLGRL MKVQYEEVAEKDDLMGVEDTAKK GFFSKPSLRSRNTIFTLGT RGSVISPT ELEAPILVPHTAQRGEQRYPF EALF RSQHYALLDNSCREYLFICEFFVVS GPAAHDLFHAVMGR TLSMTLKHLD SYLADCYDAIAVFLCIHIVLRF R NIA AKRDVPALDRYWEQVLALLWSRF ELILEMNVQSVRSTDPQRLGG LDTR PHYITRRYAEFSSALVSINQTIPNER TM\QLLGQLQV\EV\ENFVL RVGSW SFSFKGREAACVFWIQQ LWTWMLG VLME*ERAADD SKEVESFQQLLNA RTQEFIEELLSPPFGVLRWHL*KEAE ALIERGQAERLRGEEARVTQLIRGF GSSW\KSSVESLSQDVMRSFTNFN\ GT\SIIQGALTQLIQL\YHRFHRVLSQ PQLRALPARA*AHSTFHHL M
78	5575	A	79	1333	1561	PLFIQLPGLPRMLTQFNY*TNHS*SK CQD\HSVCSWVKAFWR AVVAHAC NPSTLGG*GMRITRSGVRD*TDQHG ETH
79	5576	A	80	132	356	KDKIHIIISILKKFDKI*YSLIHK\TL*K LGME*TYLNIIKVIYDRPTASIILSGE KLKSFPLKSGR*QECPLL
80	5577	A	81	108	335	NKDKIHIIISILKKFDKI*YSLIHK\TL* KLGME*TYLNIIKVIYDRPTASIILSG EKLKSFPLTSAR*QECPLL
81	5578	A	82	3	6742	
82	5579	A	83	499	1018	PTRVFSITAKLINGGVAGLVGVTCV FPIDLAKHSPQQPALGKPCYKGMIR LPDRRLGRRASSAMYRGA AVNLT LGTPEKAIKLAANDFFRLLMEDG MQRNLKMEMLAGCGAGMCQVVV TCPME*PTRVFSITAKLINGGVAGL VGVTCTVPIDLA\TRRSNQHWESH VTKE*SDCLIEDGSGGG/PSSAMYR GAAVNLT LGTPEKAIKLAANDFFRR LLMEDGMQRNLKMEMLAGCGAG MCQVVVTCPMEMLKIQLQACWTP GRPSSGLGLSTLHLQVLHNWFGFHP QAPLCHPHCLG
83	5580	A	84	3	305	GTRQGCPLSPL*FNTVLEILVRHS/RS SSSSSSSCLTADP/MVLHIENPKGSIK *VLELINEFSQVAGYKINM/QKT VAF LYTNN*LSKKEIKKTIQFIASKRT

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84	5581	A	85	39	281	KPRCIVSFFSMVVEA*ASIVK*EKEK IGNQGTKL**FEEMI/LYIGNSRASA DTLLEIKDFSKISGYRFNIHQSV MFL YFSC
85	5582	A	86	456	712	NIFTYLFIFVTESECTVVQAGVQWCD LGSLQPPLPG\SSDPHASTS*VAGIT GVSHGAWLIFFSFFPFLRRSLPLSLQ FGQQSETLF
86	5583	A	87	218	468	NNFFSSRVLLSPRLECN*SR*AHCN LR/LPGFKRFFCLSLPSSWDYRLLPP RPANFLYF/SV*TGFFHHVVQASLELL TSDDPPAL
87	5584	A	88	372	666	NVCFIRTGTDCIIEHNGMKLAITKE KLEHLQ/YVWK/LNRFLNNQGVKEE ITREIRKYFEMNENKNTKYQN*ECV MTTVCRGKFIAANVHIKKQDSNYV R
88	5585	A	89	36	350	KLQLHNLKARIAAIHQAA*LTPVIPT LWEAKAGRFLEPREVKASLGQ/P** GTHVHKTYKIARAWVAKHLWVPS YFKRLEVRRVALSPRGV/NGCS*RLI LPLPSQP
89	5586	A	90	58	375	VFYNKTTFKVFIIAICS LIYFVCLHSI VI*FFIL/CYCRVSEIFGYRCFIKLLL KSLL*L*FVPLFILFACILLF/WLNC YFLRLSTIVFF*KKLLIVLTFFFLYRS IIFS\CFYLLLF SFF\CFGCTL/CSCLC LQLCLFFSFSYFLIHVLR
90	5587	A	91	107	355	DMILYIENPKDSSKNPLGLINKYSK VAGYKINTQKSA AFL*TNNYLKN*P /MRTIPFTIAASSSYLETYLTMEVKD LYTENYKM
91	5588	A	92	31	358	NVKSGQNLTMGEGSVSQQSIFSSLG GHRTVSVVTMVRRCRCPAHRGLSR WLPST\SSGTQ*GP*NC*PNPPITLLR PPRPRQRCPSLCQFPP*TSRQRPSQ PPQGPPEFP
92	5589	A	93	1	1253	MRIPSFLNLQDFEDKMEIKRYRPE GPLATSAQSHVSTAPLISTQIPHPV PLFLDCRHLTPASLFDQTLIPKKAPS NCVTDSYRKTS EIHGPSLFLILNLQF RTSTSNCCFSGSGKEALTGSIGRERS PLLAQTFFPTLKKQSRSATLECDDEE ASLWENPLRDHGLFPASEHRLPLPL NQKGPPLRTSPA AHSPPNFAG\MP PVASSEGLTSIYSQLSPIG\PPGRRRQ RGCPY*VQLHGDWPLCTAVYT*AR RSVAL*SRFCG*QTRR*TRWQRNPP VCSG/HKLREFPLKLELFPQIQDPIG HQFVISVGQVRGH*STQKLYGPIRS ASPGAD\GGARGRRGFDCGSPPPAP NLHPGARALPGSCWSHLPGVRSQE VSFLDSGSGSRVNPTAEDEAWESG LCSSHPACQEHTKDL
93	5590	A	94	216	1374	RPQGM PVSSPPPKLLLDPLAQLFS GQQDPQPLEKPHLQCLGRELGSGR RGGGWSPGVENRSQTLFFPGHRAP

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						APGDAEGSGP*SFSGDARPTGHLLP PRKG\HL*SSGELRPGRCONSQAQFG/ HRGLGVPRGALGVSLAGSSFPSPPR RRPSG*AANNSVASEGAR*ALGRG/ GPEAMP/DEFVRGVVSGG*GPRGRSR LLIEW*TEAMFADPTRTAGGVGTD GKLLPVPQGQDH*ARPWKPREIRAVS RAGHVG/LPAC*EIPAQSLSGPARGA SAAIFGSCVPHGGSTRAGMVVRVA RGSPRGEQGLVLTR\GTTTRTCGMNS SSPLAFSPLKSPG/MGGQLAGP/PGA PSARWSHGGSAGRWCGRGVVGQE LVSWIHRSVTGSPHKFVGCWRQTS
94	5591	A	95	282	612	
95	5592	A	96	19	1153	DLTPGKWDQEQEPGRARAPGWRLG AGGGEPQSNPLFPAPRTCPRGCR NWPIKLLCNGKKPEAPGGARGASL SEPSPLPGWPWSTGSEEADLEDRT\ ERPKGFDSDHDEMVKP*NPKVPNCE GERGCSRAGSTLESPGESSAQVQE KKDYAQQWF/SNRGQLRPHMPLPT PLGH*AAAGGSGRENVIPGMCLVS GGDRCC*TPCNPRWEGPSPTPK*PF RQRWRNSRVRSIAHGILADGIHGF DQLDLGSEEKAPASEGTLEVLPRAN GGVALPVA*RWEDGRRHRLQGKV GDQLSAP\GLPGKSFLSSPPRFPHP DSL*C*GCRGLGPL*CRGCPRLTSG ASPLPPPPGNLVGGSGPGDPRPSCQ LLPPGKGHL
96	5593	A	97	429	945	KSVLSTLNWAQPRHWPETLPWVPS *PETSLEPPPGGS/APPTPDMD*LNSAS PNSAPPAC*NPSACRLSSLPATPV QDPT\PSTEQAPKPAFTPWLPAAAS\P FKAQTASKG*PSHMLPPLPLLTFT KPV\PSALLP*APSQPPKGVVPQAPS QHPLTPSHRTCSPAGLLTP
97	5594	A	98	178	603	SQHFGPRWTNHLRS*IQDHPG\QHG KTPSLLKILKKLAGHGG AHL*SQL LGRRLHENHLNPGGGGCSEPR\CHT AAWMT*DSVSKKRPGTVAHAC YPSTLGGQGGGRITRSRDRDHPCQYG ETPSLLKMQKLAGHGGTRL
98	5595	A	99	405	689	GSFLFFCFFF*DRVPPCSP\GWSAVV QQPQLTSALTSGSHLSLLSSWEHR DV\PPCPG*FFIFCRDGV/LTVLHRLV SNFWAQSILPPWPKVLGL
99	5596	A	100	3	307	FFFLEPSLACRQAECNAHLAH/CKL NSWFTPFSCLSLRNSWNYRCPPSRL GNFFVFLVETGFHCVSHDGLDLLTS *SVRLSLPKCWDYKGESLHRAQNY LDL
100	5597	A	101	279	469	PKMAQTQKGYLHLILALMCFYFRN TQAKKNLKRDC*RPSRMPKDLACC KSIQNKIKQKIGRKK
101	5598	A	102	265	446	
102	5599	A	103	283	398	NWQEKCTFQIIGGRKRMSFRILINF



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						FHN*DRTVCYVP
103	5600	A	104	283	397	NWQEKCSFQIIGGRKRMSFRIILINF FHN*DRTVCYVP
104	5601	A	105	2	1012	AEALVESFWKAKQHTKEELKSLQA KDEEKNENKAKAACSAAMEEDS EASSSTGDSSQGDNNLQKLGPDVV SVDTDSIRRVYTRLLSNEKIEIAFLN ALVYLSNPVECDL MYHKVYSQDPN YLNLFIIVMENRNLHSPEYLEMALP LFCKAMSKLPLAAQGKLIRLWSKY NADQIRRM METVQQLITYKVISNEF NSQNLVNDDDAIVAASKCLKMIYY ANAYAVTKNLGLYYDNIRMYSER RITVLYSLVQGQQLNPYLRRLIVRCD HIIDDALVRLEMITMENPADLKQFY/ RGI*RRTRWVA AFWDRASEP KANSI GFGGSQ LWMPTPVASYT
105	5602	A	106	966	3172	
106	5603	B	107	1	2271	MAGKASESWRKVKDTSCMAVTRE NEKDAKAETPDKTIRSRETYHHKNS MWETAPMIQIISQGVPTPTTHENYGS TIQDEIWCLTNFCLDDMLS FVLESC TNHCAYCLNVWYRKRAAAKHLIER YYHQLTEGCGNEACTNEFCASCPTF LRMDNNAAAIKALELYKINAKLCD PHPSKKGASSAYLENSKGAPNNSCS EIKMNKKGARIDFKDVTYLTEEKV YEILELCREREDYSPLIRVIGRVFSSA EALVQSFRKVKQHTKEELKSLQAK DEKDEDEKEKAACSAAMEEDSE ASSSRIGDSSQGDNNLQKLGPDVVS VDIDAIRRVYTRLLSNEKIETAFLNA LVYLSNPVECDLT YHNVYSRDPNY LNLFIIVMENRNLHSPEYLEMALPLF CKAMSKLPLAAQGKLIRLWSKYNA DQIRRM METFQQLITYKVISNEFNS RNLVNDDDAIVAASKCLKMVYYA NVVGGEVD TNHNEEDDEEPIESSE LTLQELLGEERRNKKGPRVDPLETE LGVKTLDCRKPLIPFEFINEPLNEA LEMDKDYTF FIVETENKFSFMTCAF ILNAVTKNLGLYYDNIRMYSERRI TVLYSLVQGQQLNPYLRRLKVR RDH IIDDALVRLEMIAMENPADLKKQLY VEFEQEQQGVDEGGVSKEFFQLVVE EIFNPDIGMFTYDESTKLFWFNPSSF ETEGQFTLIGIVLGLAIYNNCILDVH FPMGCLQEANGEKRNFSVTWETLT QFLYQSLKDLIGV*
107	5604	A	108	264	378	
108	5605	A	109	297	353	
109	5606	A	110	1034	1195	MQKKMIFQQTAPLNPVQTV*RHP TPKRKECPSLRRQSTLLRMMWYLP CDQWS
110	5607	A	111	1075	1826	LGLQNRNFGYKKHFWVLTDSEPAG VGGGEWFFFSLSRSDRSGAISPLI TLRTLA AKGAHQALTKTMEMMSD KKRI*VTFLFEFKMGRKAVETTCNI

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						NNAFGPGTANERTVRWWFT\KLCK GDEGLEDEEP*WDPLEVDSDLL\AR TIKAD\PLTT\TREVAEEFNIDHSMV FP\HLKQIGKVKKLNK*VPHEPSKN KL\FLEASSLILCINNNEPFLSRIVTW DENWILYDNH*QPAQLLD*EAPKPN LHQQ
111	5608	A	112	540	724	EAMFYTWEGEWAQEIVGLKKIRL GN\AHAYNPSTLGG*GGQIA*AQEF DTSLDNIARPVS
112	5609	A	113	1	370	QSRGRGSLRIGQTCRRDMLSQEL PRLEFPLLLLLMLLMP\PPPCPAHRA TLFDPTWESLDARQL\PAWFDQAKI GILIHVGVLTPSYCIERV*RNWQM EKIPKNVEFMTDDYPPRYTHEDF
113	5610	A	114	151	379	PFYVENP**YTLKNFLELISNYNKV AKYKINIQRSIYFLYASHKQVDFKV QTQ/LPFTLA/SL/RMK*FSISLTK*VQ D
114	5611	A	115	17	214	KQRLSYCIYKTTKTYATYKEIHR/LE VNGCKRIYHANTNQKKAGVAILISD KKHLRQEYYQG*KEML
115	5612	A	116	249	675	QYISVTRCHISMLTLNLNGSNAPLK RYSLTE*IFLNDTTV/CIPRHTDRLKV KG*RKTCYTNRKQKQ*/GAILMPD KTDVMSSSSSSSRK*IIVKGSILQED MTIQNIYTPNTIAP/R*VKLILLGLK G*IHSNTIMVGKFSIR
116	5613	A	117	67	373	FCDCHHFILMFKSPHIWPGIFSSWL LCFFWACLHHSLSIALLSCTKRYSG LILYFLCSSFEITVSSKSSVSF*RRMV FRNQVLGSRCACCC*GVAAPRPF
117	5614	A	118	366	795	AWVEQSKVLIKEGGIQLLTIVDTP GFGDAVDNSNCWQPVIKYFDSKSQ D\YLNAAESQVNRQCMPGNRV\HCCL YFIAPSGHGPHN*RLPPSGRIG*YM FVTTWHCLLLRLKPLDIEFTKHLHE KVNIPLIAKADTLMPEEC
118	5615	A	119	105	702	AGSSVSLGFCPAAAAHKPRGGALR LPVFERRAQGPDYALAGVARQPA GTCRRRCNRSHCRAEDPQWPTPAA APAAHSPHMSLGESGLGLILINSF LTDLYSPEYGPSQRIKKPVQVYILV FLIDDKLE*Y*YTQSTCCNFHYAS\Q SWQPAINYIDSKFEDYLNAESRVNR CMPGNRVQGCIFYIAPSGHGPHLH N
119	5616	B	120	7	177	MSVSARSAAAEERSVNSSTMVAQQ KNLEGYVGFANLPNQVYRKSVKRG FEFTLMVVE*
120	5617	A	121	2114	2945	KSVAF\CTNNVQVQAENHIRNVVIS VTI\APIHKIKYQRMYPKEVKELR ENYKTLMKIIDDTKKWKNIP/C*W VGRK/LIYRYNTIPIKLSTSFTELEK KILKFIWNQK/HSRIAKAIL/AQKYK AGGITLPDFKLYYKTTVTKTAW/Y WYKNRHRDQWNRNTEPEIKPYTCN

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						QLIFDKINKNKQ*GKDILFNK*CWK NWLPICRMTLGPYLSPTYKITSRW ITDLNVRLQTLNILEENLGKNLMDIS /VGKEFMTRP/PKAYATKTKIDK*DL IKLKSFC
121	5618	A	122	3	113	GLDLLAS*SARLGLPKCWDYRSDW GPGPVCGHLCRG
122	5619	A	123	145	540	FFVFFVEMGFHCVAKAQAYNIFFFF LRWSLALSPRECCGAISVHCKLRL PGSRHSPCLSLPSSWDYRRLPPRPA NFFFVFLVETGFHPC*PGMGLDLLT S/SIRPASA/FPKCW/DYRA*AIAPGK MRLFNSL
123	5620	A	124	739	835	LAKISNSDVLKLSMLHKSSENSISHK TGAERNKYLLIKLKVI*LLTL*VNIC FFQLQFYVK*SFQIYVAWKVLRQS Y*FLPVIFSIYFFYL*LIFV/CDTFCF *SHFLLFIFYVYFNLVTMRITYNILEL *HFNLNLFLQKFNHIPKFYCYIYIAL L/CFMLLM*QIISLFIVYH/VTDLLITF YAFAF*IM*KIKSRVTNQNYNRTVF MFVY\YLPPEFVYSYSLIYLHSY CLEFIYFNLKDLTLPECQ/FRDKWIF FQF*KKIRKCLNFS/CHF*RISFPAIYF SIDRFLHYFKYIIHCLLAFKVSAREIS C
124	5621	A	125	48	492	HPTGPGRRSHRPRPCRRSLTSLAPSP WPPGSLQRSLLDPQRSPWRPRTQAC TRSAHALRHTIPRSTLGVTVGLEAA PPPQHLRAKGT/PPVPGAQPPPGPRP WPTQLRERPSPEPPPPGLGLPGSKTP ALPARPRVG*MGPKAQPHTPF
125	5622	A	126	536	669	YLNVGNNVVG\PMAHTSNPSTSGG* GGWST*GQELKTILTSLVKHS
126	5623	A	127	793	829	GRCHLAHGGVQGSRIKPQQLGAWG RRQRDIGNRGSRLWGEKEEKAGE RKDEPALARSTSQAPSRLHPCIFNPL GVRYPRAWALHPQLCAPP*AHVSVS TQIPRQRPQVAVTSLVPPISG*FRAP QGKLPNGQMLYGRHHPQLQAPPTA RASPSHVLTLTGTEQPPRA*THSPEK W*GVPAWLRTSPRPRPVGRREQVT LIWKPKQN*SAES\PPSHRAYPEIPFR LLCLQPRTGPVLLGP*SSKCPEPPC\ TKSKPGWGKACSPLTGPCLPSP/PDL PSVPSPSPVLPDPNRTATASRNPTV TERYLNASLCWSQPDLPQGPIITDM PSAPAVPLTSDNCPSMSPAPSGKAV RQMPPGTWWGSG
127	5624	A	128	322	386	IRCFALRFSSLLSFIHLY*DT*HPDT* HPDIQTPGHL/HTQTPDTRTPGHPDT ETPDTQTLRRLTPRHLD*HSDTQT PDTQTPGHSTPRNL
128	5625	A	129	323	516	AGGRFPSWDPFSSRGSQASKPVRMP PTR*MRR/RGRQPCPGHRRRTQLFA VSAPSRDLQNCSRERF
129	5626	A	130	238	583	MADKQISLPAKLINGGIAG\LIGVTC

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						VFPIDLAKTRLQNGQNGQRVYTSM SDCLIKTVRSQGYFGMYRGAAVNL TLVTPEKAIKL\AANDFFRHQLF*GR AEA*PCLKRLLGGFWG
130	5627	A	131	3	492	SSGLGCAGTRDSQLSIRRLSSTRRS GGGGDGDGTPARDLQLGWLHLLH GSGDRRGIECAIKRKDQGVNQKK KKKRTSKLGRMSSCSNVCGRQAQ AAAEQGYQRYGVRSYLHQFYEDCT AS\WEHEDDFHILRSPTRRS/SYIFE GVDSFSGTLL*YLAWTG
131	5628	A	132	1	245	GPGTGPEPWTPYS*EGDPRGRPRPR PLGPPP/TAHAADGSYRHSASGPGS WTSPFPSPGGGEKSGRTGQRVWKF GFWSWLCH
132	5629	A	133	554	1049	GRTGGGLGLLHGHTRLADTDLLDR GMLKDTLAQAPPPPLGEAYCHQGP GPWAGGGALSPGTRLQAGIQG/P/PE PQLPQLRPEPRP*PP/AQVVAGCGPA DLPPGGCPGCSGCSPHR*TAFIKTSA NPATLAGVGWG*GHPEGVPHTASE TGSDLQL*PTAIGHTGGPW
133	5630	A	134	798	1083	DPVGKGNVELPGRIAHCFHCLPVLH VCLSLSVLCVCFVLFVCFSTSLF*RII VFERYLTFLVCLCC*GLCFICTCF\F YCSLVF*LFASCFLYSS
134	5631	A	135	71	484	EIFCYCVKYTYIQTHAPFKFFRFIYL FRDRVSL*PRLECCGVVLAHCNLR/ LPGPK*SSHLSSLSSWDYRRTPPMPS WFLCFS*RRGPHHVIQVGLELLGSS SLPALASQCWDYRREQWPWG*KVF LSSAYCLFHLTLY
135	5632	A	136	186	434	SQHFGPRQLDAPRSGI*DQPGQHG ETPSLLKIQKLAGHGGRRL*SQL\LE RL\AQENHLKPGGGGCSEPRSRHCIP AWVTERD
136	5633	A	137	1638	1904	GGWITRSGDRDPSLAKHGETPSLLK IYKKLAGRGGGSL*SQLRRLRQEN GINPGGRACSKPRSHHCTPAWATG DSASKK*KIKKKVV
137	5634	A	138	421	1155	KICGSYYPLFLATFSEESFQSMLIK TTLNLNVGLVLSWKR\VQGAS\GKL QGLSEFCESQGAQNLTLRALRLHLD LQIGEKLLVKVDAKTKAQLDEWK AKKKAS\NGNARPRNCHLMTDEEA LDEETKRRDQMIKGAIEVLTREYSS ELNAPSQESDHPARKKKKEKKEAIF RRFPVAPL\IPYPLITKEDISAEMED DYIDLISREISIFRDTHKRSYGD*CK MKLSAWKVTRNRINWKKRK
138	5635	A	139	338	395	
139	5636	A	140	340	1248	RPLVLANCIEVIKRIVDMQVPLISG MQ/AWFNIVKQINVIYHLNIMKDEN HIIHGEKAFHKIQHPVIMEILNKIE REGIYLNNTKTIHEMTTAEINSQGK WNAFPVGSHMMQE/CLSPLLFN/LIL AVLARAMK*/QKEIKLIEIRKKEVKL

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						YLFVDDMIFCAENHKESTKILLELS NIFSGFAQYSISTKN*LNHFTFNKQ L*KKILK/QLPLAGELK/RKKYLKIN VKRSEVFTLKSTNIDAND*KHI*RH NPY*WFGKINIVK*LYNNPM*FRFN MISIKIPISFC*RNKKQAGKMAHVC WPG
140	5637	A	141	47	411	
141	5638	A	142	1	343	GRLQAITDKRKIQEEISQRLKIEED KLKHQHLKKALREKWLDDGISSG KEQEEMKK/RKSTKEEAILKKLSIE RTTEDIIRSVKVEREERAEESEDIA NIPDLPKSYIPS
142	5639	A	143	460	976	LLRIGKEAELGGRGRLPGHSQIKRK LQEEISQK/RV*KLGEDKLKHQHF DK/VPLREKWLPRWNPASGKEPGR D*RSQNPQRPSTQIPGS*NKVSLRLE KEIQDLEKAELQISTKEEAILKKLS IERTTEDIIRSVKVEREERAEESEDIA YANIPDLPKSYIPSRLRKEIN
143	5640	A	144	79	533	SSIMTFLESSAVPPHWTGQDGRVC WTGWIPQCQAGSAPE/RS*VFINSAG QKSADTGWSSSKPQN*HLSSFHQA VVGMIQPSHSQFLMKRKAASPRKL EWEH/LQPLHPMTLLYR*DGKPF* VLLSTYTYCSSRDRPKSSGKNARRF PAHGSS
144	5641	C	145	354	416	MKESPGGELPQTGKKPVFLF*
145	5642	A	146	3	145	SSSSSDFAGQTL*STQTVQN*FKKVL KPGRLYPVPIATMGIKEPLIS
146	5643	A	147	214	464	FCGLLLLHPVSADF*PAELINTQEPQ ERCQLDTGESSRVQHTLPSCPVCQG GTAELSRNVMIGASELKCLHPSPKL EYILPGN
147	5644	A	148	246	730	SSIMTFLESSAVPPHWTGQDGRVC WTGWIPQCQAGSAPE/RS*VFINSAG QKSADTGWSSSKPQN*QLSSTGAAL PLASLSRERAW/VDDGKHRLTTPMT VPQRAVQQI*ETSG**DWRQKVQIF QQA VVGMIQPSHSQFLQREDVIML RPFGLHLSWEENG
148	5645	A	149	12	288	FGGGYIPTWGKGEGILALELNHDIS REFCSAPALASRPPPTPPPLLPPT/PP LPAPRSPADATPRRVGGPLR*ALKP RAPGPGWSRRRCRSWW
149	5646	A	152	106	344	KQILLPPRLEG/NGQNSG*WKFLP GPSLFCPSFQTSNGYGPQQARAIF WKFKIKTGFGVTRGLNFLTSGSA PLGS
150	5647	A	153	38	349	RTAKSGSTKFSLSNKGTVLAVLF MKKILVRLSPKKNDQTVKYIKRPL TSLKIREIHIKTALLYLLE*KLKLF DDTCH**A\WRNYCWRVCVLIQPL WRQMW
151	5648	A	154	220	970	ESRTRGAEAAAGLAPSTSPQAHGPA PLPTHVCCGVAIGMEPGHTAISPVV ELAVHLTGLVSSHDLGMMPSQQG

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						*QWGRQRGLASGN*GRMSFPNSWP VTPICAARLPPGLLLICGFDGAGHSD RSEGF*GLRFPFCFKRQ/RSHSVSQA RV*WCDHGSLQPPSSGLK/HPPVSA SQVAGTTGMWHRAWLVCLFETES CSVAQARVQWRDLGSLQPLRPGFK QSSCLSLSSWDYRHHVAPCLASLFV CLRRS
152	5649	A	155	193	369	HLN**FSNLIFFETESPSVTRGIISAH RNPRLPGSSDSPTSASRVAGTTDT
153	5650	A	156	626	1017	FDSCFLFCFVCLRQ/VSSVAQAGVK WHGLSSLQVPPPGFTFWSLSLRSS WDYRHPSPHLANVFCFLGFFVFLVE RGF\TVLAR\IVSIS*PHDPPTASQN AGITGVSHCAWPTLVCLNAKFSIVV FVHKD
154	5651	A	157	1	336	TVSQAPSPESNPHGRRGDYHRKLIG QTFEWV/VRRHGGRAIGPRLSRVTK AAGARPEPKDFGFPEAARRVMGIT PVLDLGRQPVRGALVELRGAGHWR AGGGTGSCGIPARL
155	5652	A	158	2	320	VVAVSQAPSPE/SEP*FPVTRGHHGR HG DYHRKLIGQTFEWV/VRRHGGRA AIGPRLSRVTKAAGARPPAGAGEG/ LDRVGFDLINARIPPAKGANGSSPPR GACDRPEVI
156	5653	C	159	177	380	MPTGADPLRGGDACIYQIKTNPVSP SPAPAGGRAPAALVTLNGLPIARP PWRRRPIRTSAPINFRW*
157	5654	C	160	1	417	MDATCHGCLQFQIMRNKKFQLLSP SSQHFRMTASGGKQLLCRTGQKM EHPIPXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXGRPV *
158	5655	C	161	1	403	MDATCHGCLQFQIMRNKKFQLLSP SSQHFRMTASGGKQLLCRTGQKM EHPIPXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXX*
159	5656	A	162	513	1086	QPQVASSYSAGQGRRWNTPSLGKIT RSGDRDHPG*HSETPSLLKIQLAG CGGRHL*SQLLRRLRQENGVNLLGG GGCSEPLRHCTPAWATE*DSISKK REKKKKKKERKKKKRKKKKWKKE RGRGEAGEEQEEEEGERRRDKKKK EKKEREETREGRRRRRRRKKKKR RRKKKEERTTKRRRRRTRKKK
160	5657	A	163	2	935	WRRSTPAPSATSASPSRRCL*SQLLG RMRQENRLNLGGGCSEPRSCHCT LASPAGTQSCSRCTSQQGVQSDIPC TAAAPETAPRRGSAGGTWCRRRAP P
161	5658	A	164	34	1026	LLALGQSSCL*SQLLGRMRQENRLN LGGGCSEPRSCHCTLASPAGTQSC

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						SRCTSQQGVQSDIPCTAAAPETAPR RGSAGGTWCRRRAP
162	5659	A	165	45	69	RKNQRIYQIARKRLNEMARISPLRS MIILNVSGLNFLKRCRLAEWTISSP DPIICCL/QKTHFTG/KDIYRLKIKGW KKIFHANGSQ*QTAMMNTNRERTK GYTK
163	5660	A	166	48	72	RKGQRISEIAIKRLNKMARISPLISII LNVSGLNFLKRYRRAEWTISSPDP IICCL/QKTHFTG/KDIYRLKIKGWK KIFHTNGSQ*RTAISQSAMCNNNRE RVKGFPK
164	5661	A	167	118	639	ATVPSQQLIFDKDSKAIQWRDTLNFN KWCY*IN*ISTCKKLDIDSYLAPR\T KINPKRILDLNVKPKTIKCLQENTGE NCWDFGSGKHFLDMTPKMQSTK*Q ISKLIKI*NFSSKTQHFALLIIRIF*KTL LTGSKYKATTWKK/VFVNHIPDKRL ISQIYQELFRTQTKNPTSDW
165	5662	A	169	435	808	KNLCNNKKFHRDEGWAQCLTPVIP ALSEARSRLYHLR\SGVRN*PGQHG *KHGLYWIMQNLAGRGGTCL*SQL LGQLRQENSLNLQGGGCSEPRSRHC TPAWVTERDSVSTTTTKIFTRMNLN R
166	5663	A	170	167	197	VKFHKIKLDGEDTTYGGFDGPGLM Y\YYLISSDGH*FTQLHQEL
167	5664	A	171	45	259	ARMNSKLALA\*ALQKRSRLRHQSNV FSMFDQSQIQEFKEAFNMIDQNRDG FIDKEDLHDMLASLGELGQQQG
168	5665	A	172	90	468	IMKLLTRAGSFSRFYSLKVGPKAK ATAAPAGAPPQPQDLEFTKLPKGW LIAPLENYPPG**IGWFIKAGT*SEDF NALGTTHLLSTTCSVTNGASSFTIT RGIESADGPLTVTASREYMDHTVE
169	5666	B	173	89	186	XLKYFQTVTDYGKDLMEKVKSP ELQAEAKVLL*
170	5667	B	174	85	298	XLEGALVRRQAKEPCVESLVSQYF QTVTDYGKDLMEKVKSP ELQAEAKSYFEKSKEQLDTPDQEGWERELV*
171	5668	C	175	279	533	MAKDLMGEGPRTPELHAERQVFTF EKFKGSSLTPLDPRKAWERELGLTS LELIFRGNFGNHSLATPVESFPRTIW SFQTPGWAF*
172	5669	C	176	260	389	MDFFAQKKKKKVCMYVHMSTQR WLPNETNQNNINVLGFLNFLSC*
173	5670	A	177	84	1008	KVCCRYRKANGGKGSPVQEVDPDG APEGAPLQQGP\PGWLPLPTTQSVS APPGGESPTENQPMFKQTDPMKS FWTKMGSPTLSPNSV\AVSHFPSPH FISN*EWEQNQPLSLVLSGRGDELH SDGGQKTQGLDKQQLPRGWHGLV SFGRAACSKLGKNLRPQEIKWSSKL HLPIPESQC*SPLVGVEQWGGKLG S VGLLLQPKGGIPTALSPALPAGHP TLPYGNNAAGTDLRLHTEPEGPHGEP GLPARWGQDGMEPRWAAAGLGKG

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						YLLQASRGVVGSETGQVGFLLFGKKT KSNRLIAVNDVSHFLL
174	5671	A	178	79	336	NCCNTIKSISEKP/LANSIR*AKKQEG FFQISGIRQGCLLSSFLFIILEVLARG NR*D/IKCIQIGKKKVKLSLSETMR FNIWKRLR
175	5672	A	179	3	370	SVCVRAHESVVKSEDFSLPAYMDR RDHPLPEVAHVKHLASQKALKEK EKASWSSLSMDEKVELYRIKFESF AEMNRGSNEWKTVVGGAMFFIGFT ALVIMWQKHVGLASKWDYEKNE WKK
176	5673	A	180	24	1173	RAVAAGSGGRMLATRVFSLVGKRA ISTSVCVRAHESVVKSEDFSLPAYM DRRDHPLPEVAHVKHLASQKALK EKEKASWSSLSMDEKVE/LWVLKG PTGAPSSSRKRVCDRAHFWAYC LESSLAQEGCSAGVSGHCARAPVY VLTSHLALPADRIFC*APFSVLGGGS LSAYLLGKT*LTVNY*KKLITMHSV WDERGRKITGLNRP*YCNSKK*FC SFNLHLKRTVCIFFLPCPVTCRLGHV CARMCVNMMWPGLVYPSALCFL HKCGFGEKWLNVAEEGAADLCAC KWLSSLPPVYRIKFESFAEMNRGS NEWKTVVGGAMFFIGFTALVIMWQ RHYVYGPLPQSFDKEWVAKQTKR MLDMKVNPIQGLASKWDRV
177	5674	A	181	1	738	RRSQRYPFPLHGDRLAAGCGRSLPR SRGAPRRGLALFRSDTGCRGRSRQ GSGGRMLAYQGYFTLVGKRAISTS V\CVRA\HESVVKSEALFASQPYMH RR*HHPCE\VAHVK\HLSCQPEGT* KEKEKAFLEASLSM\DEKVEVVFAL KFKE\SFA*RLNKGAPNRVVGKDRFV WAGAIVSFNRVFTALRLSCWQK\H YV\YGPLPRKSF*QKSGLAKQTQEG CLDNEGEPPSQGLASK\WPYEKNE\ WKK
178	5675	A	182	82	395	ICSFAPSSIFWGSFTGTCSSTSVRA AAPPGTPQRPSMDAHMTGRKGRLS *TSFFTWSMVTALLGVWTSVSVVW FDLADYDD*L*ALAIYDADGDVRF LRGLSH
179	5676	A	183	134	594	VITLTVSPALVANNARSGLTLPAP/P LPTGSRRTG\PSWEPDGLGSSLASC *NPPGAPGPKS*SQTGRPALPALASR LSGPLLQLPCFLSVPRSPERAPGPRH KLLLLQSLMAVSFISQFKCHLPGEV LPDRAAPGGSWPGDSRALTKSPCT
180	5677	A	184	3	404	
181	5678	A	185	2	851	AAAPAPAPAPTPTPEEGPDAGWGD RIPLEILVQIFGLLVAADGPMPLGR AARVCRRWQEAASQPALWHTVTL SSPLVGRPAKGG\VKAEKKLLASLE WLMPNRFSQLQRLTLHWKSQVHP VLKLVGECCPRLTFLKLSGCHGVTA DALVMLAKACCQLHSLDLQHS MV



SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						ESTAVVSFLEEAGSRMRKLWLTYSSTAILGDLLGSCCPQLQVLEVSTGINRNSIPLQLPVEALQKGCPQLQVLRLLNLMWLPKPPGRGVAPGPGFPSLEELCLASSTCNFVS
182	5679	A	186	2	568	EFGKDSCGNISAALPPLSAQVFTAPEADPHPLEVSGTIPRVEGESSL* LHITCDTLGLVSTLGSGSGTLGAQRCSVMSACLPGLSLFLLFPAGRYQRRGHP SRPGMGRKEVTAKAVRVGLAPATLSVSLVDLSLSSPNPSCPSVSPQLVGECCPRLTFLKLSG\CHGVTCLTLWSC LAKACCQFHKPW
183	5680	A	187	2	333	ARDSTSTTEMNPQVLFQRV**QFL LITTSWRKVISQTFGRLLVDTGSKL/TVQMPRISSPSVRVAACGGQVIDGVLLKVQLTVDP*T*WTDLVIFS/SAFE*VIGIDILGSECS
184	5681	A	188	2	363	AREVFTQHS\HLTYH*TIHTGEKPYK CIECGTAFGVRSLSIHLVVHTG*LPYRCHCEGMVFMNRNTHLVRHQLIHT GEKPYMCNECGRAFIHSLATHQAIHTGEKPYICTECGTVFTQN
185	5682	A	189	361	1026	RKYLPPRPTFNALPLKVRWGRGLISKLYH*LYQEL*L*LYQGLITILLE KKLI*KLDKNLNRHFSKEDIQMANRHMKMYSTSLNIREMQIKTMRYPSPPQLKYLLSQKTGNNKC*RGCGEKG TLVH/WWKCILVQPLWRTVWRYL/RKLKIELPYNPAIPLVGIYPKERKSVY*R*ICSMFTVALLAIAKIWKQSKCP SADEWINKIYAYTTEYYSAIK
186	5683	A	190	158	366	FIISMNFVFLYFVFDLSINEILLGLKE WSIYLSS/DHSLSSLCSEFYLLLMFFLCMLLLLLLCSSIIIS*P
187	5684	A	191	10	284	
188	5685	A	192	3	438	LFISLLSISEKIIENCWV*LSAARS* ALRKLAFF*ATRSFF*ARDILGRFHLFF/CNFFLGLLFIDWILSYSSMSFLIHL LHPAGQQQASTICCSIIQANLHTIFWQFVCIRCADYHIPLYTGISNLNDISVCHTNYHPVIGVW
189	5686	A	193	497	752	DGVLLLLPRLECNSAILAHRNLRPL/GFKRFSCLTLLSPWDYRHLPPRLAIF FVFLVYVGFHHVGYAGLELLTSR*SARPRPPKIA
190	5687	B	194	922	2057	YPNRFPLVMDSEKQRNFNAESTIGSHIHGPRIVAGLHAPTLMEEDDALQ ETVRASIRKEQRNSRHDGGDGIRKAHAAPRESRSMKRSRKEVKKKRW NRPKMSLAQKKDRVAQKKASFLRAQERAAES*
191	5688	A	195	1492	1790	SQTLGGRGGQITKSGDREHPG*HSETPSLLKIQ\LAGHNGCLWSQLIRRL RQENDMNPGGRCSEPRSCHCTPAWVTEQDSISKKKKQKQKEGLGGS A

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192	5689	A	196	178	572	QAGSCTRTSQPRDSRGSDIQPVGLA FGRTPAELQELHLSSPRPGRGAVWA CGSLEPGPLPLLSITSGSQPSLQSSL PQSPLFCPLPPF/PPPRPPPRVGLVPPP *LTHVPG LQPTGRPPPSPSRSPAPP Q
193	5690	A	197	209	684	PWDCVHACLRGGWHSANRGHFRI GGPGRPKAPFLPPASLKVQALIPYP GVHPGRPLHPCVPRRMQRLCGTRD PEKLASCDIVVDVGGEYDPS\RHRY DHHQRSFTETMSSL/DPLGSRGKTK LSSAGLIYLFHGAQ\VLAQLLG TSEE DSMVGTL YDKMY
194	5691	A	198	2	720	IPGCMIRHELLPPCRELLMGHRFLR GLLTLLPPPPLYTRHRMLGPESVPP PKRSRSLKMAPPRIGTHNGTFHCDE ALACALLRLLPEYRDAEIVRTRDPE KLR\SCDIVVNVGGEYDPS\RHRYD HPQRSFTETMSSLSPGKPWQTKLSS AGLIYLFHGHKL\VAQLLG TSEEDS MVG\TLYDKMYENFVEEVDAVDN GISQWAEGEPRYALTTTLSARDARL NPTWNHPDQDTEAGFKRA
195	5692	A	199	209	684	PWDCVHACLRGGWHSANRGHFRI GGPGRPKAPFLPPASLKVQALIPYP GVHPGRPLHPCVPRRMQRLCGTRD PEKLASCDIVVDVGGEYDPS\RHRY DHHQRSFTETMSSL/DPLGSRGKTK LSSAGLIYLFHGAQ\VLAQLLG TSEE DSMVGTL YDKMY
196	5693	A	200	2	720	IPGCMIRHELLPPCRELLMGHRFLR GLLTLLPPPPLYTRHRMLGPESVPP PKRSRSLKMAPPRIGTHNGTFHCDE ALACALLRLLPEYRDAEIVRTRDPE KLR\SCDIVVNVGGEYDPS\RHRYD HPQRSFTETMSSLSPGKPWQTKLSS AGLIYLFHGHKL\VAQLLG TSEEDS MVG\TLYDKMYENFVEEVDAVDN GISQWAEGEPRYALTTTLSARDARL NPTWNHPDQDTEAGFKRA
197	5694	A	201	94	660	LHLKNSDGYCLIVYQKRFPVTFIHF CFLILSLKFNNIPLNIFANGEKYFVY KFTYSY\YVVKFLTC\FVELPVNCLFI SFSSHFLMSFVIFL**ILGMLYVLVL LIFNFTYICIVIAFY*LFVVIQTF LHFY LLKFINLFL*SFGFCVLLRRVIPRI YICFIRILYNTSITLFTYLEE*FSFDM
198	5695	A	202	3	347	FFEMEF/SLLLPRLECNGVILVHCNL RLPGSNDSPASAS*VAEIGVCTASS *IFVFGTLTQ*KSRLVDQAGLELL\ PASSDPILTSQSAGITGVTTDIQPPF FLSSFANTEWT
199	5696	A	203	32	403	APIPDAMGHFTEEDKATITSLWGKV NVEDAGGETLGKLLVVPWTQRFF DRFGNLSSASAIMGRR*VKAPG*NV LTS LGDALMHLDDLKAPLANLRER T/CDQGCWVNPENF*LLGNVLVTVL AI

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
200	5697	A	204	94	361	FCQLDSLYTESQSLDSTVL*LAEHM KFIKTSYD*GALDTFTKHLQMSVDA YE**MISILNPSSLSERQSLLLFIVLD LSLVPYLLIFE
201	5698	C	205	265	408	MTLSCSNLVFFFLFKITVFIMTMVTP QCKGGPDSVCFSTLFFVVKCPV*
202	5699	A	206	10	419	MRGGHSHWARKGGMRGLRNERES GGGEQTD*ASKLKRGNNSRITPFAY MDTY\ASSSSSSSSSSSSSSSSSSASKLE AELGQTGLLPIPLGGGGGAFSTKT RSGESEGGLWKQRKRWSLEGRRCGR VSGWECGGAEAMK
203	5700	C	207	165	248	MDTYXXXXXXXXXXXXXXXXXXXXX FQARS*
204	5701	C	208	337	428	MILRVDDFVPLALLPQSFPHRSHYD PNPAA*
205	5702	A	209	531	1860	PSKPPNQCFLSLSQATSAGTHLSQD TESLTQVAKGIS*GSQGHGGGTL*M RGGHSHWARKGG/H*EGSSGMRGRA VEGNKQTRLN*NGEIQTELPLLHT WTLTVQMRKVTPREGELSCPRASK LEAELGQTGLLPIPLGGGGGALSTK TVRSG\GVRGVFGSRENDGLWKVD VEGSVAGSRAGA*AMKGEPKQIPK LTL*S*P*ENPNGNAVFS*ARGKL*/ SFTKTLGAPAGAPAPAPP\GPRWPP PA/DCGHTRPPLPSESLEAELKAGDS PSLALDSLSP*PPPTPPAGPRRSQGP GAPAGALGSRCPQQVKQTTLGS* RGRAGAGNTRRRGSGPHAAPIGSV DLRSGAPATAGPCG\RAASVAGAPR RGRGGRG\LPAPPWGT*GAPKGPRR RGPAGWSQTGSARPCGPWASRGGP KPRPCVHGGRRPGDAPGVVTPARC GR
206	5703	A	210	32	452	
207	5704	A	211	38	618	APSPDAMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF FDSFGNLSS\PSAIMGNPKVKAHGK KVLTSLG\DAIKHLG*SQRAPFAQA* SELALVTKLHV\DPGGTFKLLGEML LVTRFWAIPFSAKEFHPWRLQAISW QKQKMAEDGDLELASALVPSRLPL SSLAHECRAFQGYGFILASNYK
208	5705	A	212	137	368	DGVYLWTHRPYCGLGSLNFGSVIIV LP*VKAYGWMVLTSLGDAIQPLAD PECSF\GQLRELRCMDLHVDPEDFR LLGK
209	5706	A	213	60	317	FPCLVCCTLQENSGKPILCPRRTAQ LGPRRNPAWSLQAGRLFSTQTAED KEEHLHSIISS*SVQDYT\SKHKFQA STYKH*SIA
210	5707	A	214	3	406	HEDKLCTVATLRETYGEMADCCAK HEPERNECFLQHTDYNANLSRLMR PEEDVMCTAFHDNEETFLKKYLYDI ARRHPYFYDPELLIFANRHKAFTD CSQAGD*AAWLVPKLDDYLYEL*A

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211	5708	A	215	1	2953	TSCIIISKCANL MKWVTFISLLFLFSSAYSRGVFRRT PLGPASSLPQSFLKCLEQVRKIQGD GAALQEKLCA TYKLCHPEELVLLG HSLGIPWAPLSSCPSQALQLAGCLS QLHSGFLYQGLLQALEGISPELGPT LDTLQLDVADFATTIWQQMEELGM APALOPTQGAMPAFASAFQRRAGG VLVASHLQSFLEVSYRVLRLHAQPG GGGDAHKSEVAHRFKDLG EEDFT ALVLIAFAQYLQQ*PFEDHVKLANE ATEFAKTCVADESA\ENCDKSLHTL FG\DKLCTVATL\RETYG\EMADC\C AKQGT*GEMECFFATQRMNDPNLP PIGWRTRGWMWMLHCFFHDNEGD IF*KKYLLWKLPGRTSFTFYGPPELL FLWLKR/RIKAGFLQEC\CQGWLD*S WPACLA KGSDLSGMKGKAS\SAK QRLKCASLQKIWEKELSKPWAVAR LSQRFPAEFAEVSKLVTDLT KVHT ECCHG\DLLECADDRA\DLA\KYICE\ NQDSISSKLKECC\EKPLLE*FH\CLA EVENDEMP\ADLPSLAADF\VEN\KD V\CKNYAEAKDVFLGMFLYEYARR HPDYSVVLLRLAKTYETTLEKCCA AADPHECYAKVFDEFKPLVEEPQN LIKQNCLEFEQLGEYKFQNALLVRY TKKVPQVSTPTLVEVSRNLGKVG KCKKHPEAKRMPCAEDYLSVVLNQ LCVLHEKTPVSDRVTKCTESLVNR RPCFSALEVDETYVPKEFNAETTF HADICTLSEKERQIKKQTALVELVK HKPKATKEQLKAVMDDFAAFVEK CCKADDKETCFAEKGKLVAAASQA ALGLTPLGPASSLPQSFLKCLEQV RKIQGDGAALQEKLCA TYKLCHPE ELVLLGHSLGIPWAPLSSCPSQALQ LAGCLS QLHSGFLYQGLLQALEGI SPELGPTLDTLQLDVADFATTIWQQ MEELGMAPALOPTQGAMPAFASAF QRRAGGV LVASHLQSFLEVSYRVL RLHAQP
212	5709	A	216	1060	1259	TKFGQH GKTPSLLKI*KL AGHGGAH L\KSQLPGRHENHLNPGGGGCSEPR LCHCTPAWVTKRDCLKK
213	5710	A	217	2	354	SAAAGQGEENQLEASLDALLSQA DLKNSL/EEFHLQVGERVWPADLLN TLNKVLKHEKTPLFRNQVIPLVLS DRDEDLMRQTEGRVPVFSHEVVPD HLRTKPDPEVEEQEKQLTTV
214	5711	A	218	90	329	
215	5712	A	219	2	632	QPSFLCVILVYLGDPVPIGA EKRRS TLEASLDALLSQA*SEELSGEFHL QVG\DEYGRLTWPSVLD SICLAFLD SMNTLNKVLKHEKTPAVP*PGHHSS GCCLQDRR*KISCRQT*KDGCLFSA H*GKSLDHLEKPSLDP*KLEE QEKQ LTTDCSPA FGADAAQKQIQSFE*NV

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						FQTF LGENQQRGSEDSWRFSGRT SRLLTPTDT
216	5713	C	220	309	479	MIHYSSSYFKSSRELHIKFKFPVST SCGAFGSKIKWKVLSEVVEETQESE QPEVL*
217	5714	A	221	76	525	PQPLGPQPQQRPSRLASCCGAAAPC SWVEGAIGHAPPHGLPIMSNGYRTL SQHLNDLKKENFSLKLRIYFLEERM QQKYEASR\EDIYKRNTTELKVEVES LKRELQDKKQHLDKTWADVENLN SQNEAELRPQFEERQQETEHVYELL EK
218	5715	A	222	534	1310	PRNEFTQQFCFIDSFFLVTLKIEALQ CSHRSRRSGEKVPPVQTYSLRAFEK PPQVQTQALRDFEKHLNDL\KKENF SLNVRIYFLEERMQQKYEASREDIY KR\NTELKVEVESLKRELQDKKQPS GLKPWA\DVENLQPVQNEAELRRQ FEEP\QQE\TEHVYEL\LENKMQLLA RRNSRLATE*TMRGWQLLVERQRK GV*TWKLSGET*RESPKNWGRCP EPQVKPDPLHLRPLAQKGKDLKKI MLGSPNHIKNASDQ
219	5716	A	223	32	360	TGSKIRNIKGIIHGREEMKLILFTNYI LVCRE/NPKIMFKLLALISRY*ATVA GCNIYIPPTPKLNFDIVG*ILLAKKLF TNANNNIRYLGINLIINDGHHLSKEI YIISL
220	5717	A	224	2	761	APTPTGQRVVRATPAQSAPVRLRRR SYDVNNPIPSNLKSEAKKAAKILRE FT\ETSRNGPDKNIPGSTVIAKAK\G LANSCLLNQSPGSLVTFQRGPGVL VARL\PDGK\WSSPFS\ALGIAGFG\G GFEIGI*GIQTLVILEF/DDPCC*EAF AKGGNLTGGNLTVAVGPLGRNLE GNV\ALRSSAAVFTYCKSRGLFAGV SLEGSLIERKETNRKSVQVKVILIE SVMRK*YFKS*YNLQSTFIYSFYNM WF
221	5718	A	225	299	541	SQHFGRLTQADHLKS*VQDRPGQH GEIPSLQKIQKLAGHGGASL*SQLLG RLRQENHLNPGGGGCSEP\RTPGWA TE*DSV
222	5719	A	226	198	660	LLLALLFNTVLRFTVCLFLFQAPILK SPCCSAARVDRRKSIWVDGL*ICSR LSK*VIC*LGTFKFVVQILQHTLSN *L/HLNIEKN*GLTG*VSILCKCLFYH SL*PLL*VKCSLRPGVVTHTCNLSTL GGRGGRIT*VQEFETSLGNIVRHRI
223	5720	A	227	1	347	GERLAGRRRKMAVESRVTREEIGN DS*KPIDREKTCPLSLRAFTTNNGR HHRMDDFSRGNVPYSELQTYTWM DAT\KDLTSLAQELYPQATLNGTH FTFAVALTHATPPGSRVND
224	5721	A	228	3	225	SCQGERLAGRWRKMAVESRV\TQE EIKKEPEKPIDREKTCPLLRVFTTN NGRHHRMDEFSGRWSKAPGKQK

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						GP
225	5722	A	229	1984	2676	
226	5723	A	230	2	590	GCRNSARGKMAVESRVTTQEEINKKE PEKPIDREKTCPLLLRVFT\TNNGR\ HHRNGRVSPRGNVPSTELQIFPLGW MPTLKELTSL\VKEVYPEARKKKGTH FNFAIVFNRLCKVPGYR*FSFLQS* GGLASTHVWAERGLDDSHPELQSR KF\QIGDYL\DIATPPNR\APPPSG\R MRPYLNSNFTYLFIFYFFPSVM
227	5724	A	231	1	291	
228	5725	A	232	3	320	AKNRLQILKFCLHFKERKTVLP SKH AVPEVIEDFLCNFLIKMGMTRTLDC L/QASEWYELIQKGVTELRTVGNVP DVYTQIMLLENENKNLKKDLKHYK QAAEYVIF
229	5726	A	233	209	461	
230	5727	A	234	104	609	RQPGTRGTRRTRWRLEGAYYLEQV TITEASEDDYEEYEEVTC*F*IPDDNF SIPEGEEDLAKAIQMAQEATDTEIL ERKTVLP SKHAVP*VIEDFL/RCNFL DQNGELTRTLDCFQSEWYELIQKG VTELITVGNVPDVYTQIMLLENENK NL*KDLKHYKQAAEYVIF
231	5728	A	235	222	502	TSLIKHYISNLFINSVEYKQ*WFL LWLCVSLKC*LGQAWWAQACNLS TL*GPRWAADHLRSEVRDRTG\QH GETPSL/LKNTKISWAW*WVPV
232	5729	A	236	565	779	APGVRD*PGQHGENLSLQK*KLKK LAGHGGIHLCLFQLRRPRQKYRLSP EGQDCSE/PMVCTLA WATEQDPVS
233	5730	A	238	656	923	VPVHRGKERGGIQDLDEIATPTLLS KSSSFKTSYCTDFFLFLTESCCVTR LECSGMISAHCSCLPGSSNSAPTSP VSHNKDRLLHL
234	5731	A	240	171	373	AWLCANKTLFLNFYLFETRSC/SLS RLECNAIIAHCSLLPGPSDSPTSA SQVAGTTRTCHDTQPI
235	5732	A	241	915	1283	QRQGRGLWDNEEGEIGTKYSSFKI DTVEKLFLGGGRSRVKPRGSNKAR DPPSFPSPAWEVGPQLGVPLKSPCG LHLGLAAVPLYDPRGGGPHTPPHTP P/PTPHIPPHPPHTKHTPTNTQ
236	5733	A	242	555	767	NKKDLFSLRSGDQKSKVKTSEGPRL /PLRGIRENP/CPPVPAPGGPRHCLAC GGITPVSAIITRISCLYSN
237	5734	A	243	2	744	GTMAVFVLLALVAGVLGNEFTIL KSPGSVVFRNGNWPIPERIPNVAA LSMGFSVKEDLSWPGLAVGNLFHR PRATVMVMVKGVNKLALPPGSVIS YPLENAVPFILDSVANSIHSLSFSEETP VVLQLAPTEERVYMRKANSLFEY LSITFLQLHNRLFQKNSVLTSLPLTS LNNNNELHLLFF/S*LQPLH*ISNFLS CDKHFTQKMIVLINNHSNLPMLPTK FGNPFLT KSFSPFNLSLKPFSA
238	5735	B	244	385	544	MTGSPEDDETGYPLRSPGQERSST

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						EKPMDNAATSGIRSPGIGQFPFRKTTDPX*
239	5736	A	245	1	449	GNEFSILKSPGSVVFRNGNWPIPIGER IPDVAALSMGFSVKEDLSWPG LAV GNLFHRPRATVMVMVKG VNK LAL PPG\SVISYPLAENVDLLFLSELQVLH DISSLLSRHK\HLAKGSILPDLYSLAE RAGFGMEIGKRYGEDSEQFRDASKI
240	5737	A	246	2	1230	GAGRVRARHLLTLRLSPCPAGPFRV APQCCGRRGTMAVFVLLALVAG VLGNEFSILKSPGSVVFR\NGNWPIPI RE\RDPPDVAAI/SPMGFSVKEDLSW PG\LA VGNLFHRPRATVMGDG*RG VNKTWLYPQGSV\SYPLE\NAV PFS LDQCLQIPIHFLIFLEETSCLFLQLGF PVRE\RVVLWL GKANFSV*RTFSVT LARQLR/NIRLVFKENSVSSVSLPLNS LSRNNEVDLLFLSELQV\LHDISSLL SRHKHLAK\DHSPDLYFTG SWAG\A DEIG\KALLGEDSEQFRDASKILVD\ ALQKFVADDMYSLYGG\NAV V\ELV TVQSF\DTSL\IREGQGTYSLEGK TSA GTPASPYNLAYKYNFEYSVVFNMV LWIMI\ALALA\VIITSYNIWNMDPG YDSIHYRMTNQKIRMD
241	5738	A	247	1547	1965	AQGRFQALCSLVAVRAWGWPLSG NSFSCGNSQCVTKVNRSVTTRRTAP MGPTRRMRVWLAASWRMAGRIVG GMEASPGSFRGKPAFERTRSTSVGR HHQRQPLRS*NHRFQDPTKWVAYV VRPTSAARRPAPCGPSKKA
242	5739	A	248	403	734	MAVQAGTQCLVQQLHSGFLQHLW LDHCRPRKMLTEVLLLEVAPA*DQA LLAGWEDVCGSREAHGLD\GRPKG RGLVSSSTATSKSAVSALYRGCLTI WTTWARTVLASEPLR
243	5740	A	249	1	552	MVWSSQRCCRKHCGAAGPGTVCQ LVRPLLTD RMVCAGYLDGKVD PAR PQKNTDTSVSNAGRFTDIWMPVLE EFKAVGIERQNVGPGLNGEAHPGR GRVRSCLREVPWQVSLKEGSRHFC EQLWWGTAGCCLPPTASPVSGIKA L/YESELADARRVLD ETARERARLQ IEIGKLRAELDEVNKR
244	5741	A	250	63	497	LPDVEKLGRRRGRKMDSVEKGAAR LR\PNPRGRPSRGRPPKLQRNSRGG QGRGVEKPPHLAALILARGGSK\GIP LKNIKHLAGVPLIGWVLRAALDSG AFQRCACARVGGA AWAGVGRGSR AAGGAGASGATALGRGPSLMPGM C
245	5742	A	251	1	349	GTRAVVCGRRLISVREQIRHFVMRP EINTNHLDKQVQVLLAEMCILIDEL DN\QAYCETKKNCHLNENIEKGAAL KQTL LLSDL CRHFRFAEKSTLFKEV QTSVIPYFLVGSSSFK
246	5743	A	252	2	423	LRWSL/DSVAQAGVQWGD LGSLQA PPPGFTPFSCLRLPSSWDYRCQPRT

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						*RRGFIVLARMVISIS*PCDPPASASQ SAGIIGM/SHRARPGFPT/CQTTQEPG GTTSHGYRIPPP*QDLC*LPQFPERG SGSQRC*DKPGSPSL
247	5744	A	253	891	1564	SPRALAANPWWMVTSVSSRVKQSC TQQGGFVPLAQQVHSPHSELYALV SLFFYFLFDICRARILSGSFCILRTL LLLFLRRSLNSVTQAGVQWRDLGS LQAPPPGFTPFSLSLPSSWDYRRLP PRPANFVFLVETGFHRDETRIVSI S\GPRDPPASASQSAGITGVNHRAW PTFCIFCRDRVSSCWPGWSRSHTPG LKRSSCLSLPKFWDYRHKLPYP
248	5745	A	254	6	338	MEPSCGLGSEALALTQTWAGSHSL KYFHTSVSRPGRGEPFIYGVYVDD TQLVRLDND/APSPKMVPRAPWIEH EGSKIWDRETHIAKDTRQIFRVNLR TLRSYYDQIEAGD
249	5746	A	255	2	424	
250	5747	A	256	25	486	EFHRLRENPPWCLSPADKTNVKA\A WG\KVGAAHAVRSMCAEALERMFLS FPTTKTYFPHFDLSHGSAQV*GATG KKVADALTNAVAHVDDMPN\ALS AL\SDLHAHKL\RVDPVQLSSS*SHC LLG*PWPAHLPRPSFTPGGCTPSLG QVSWAFC
251	5748	A	257	230	358	FLIILRRSLILSPRLECNGSVPAHCSL/ RTPGFKRFSCLSLSSS
252	5749	A	258	75	188	
253	5750	A	259	340	535	FRFKALFDLFLVEIASCCVAQAGV QWCDLSSVQPPPGSSDSPTSASQI AGTTGALQHAWLIF
254	5751	A	260	1618	1962	DRVSLSPRLECSGTL\AHCKLR/LP GFTLFSCLSL\PSSWDYRRLPPRPAN FFVFLV\EMGFHRVSQ/AMGLDLLT SGDPPASGLSKCWGLQGVSNLRPS QASPSFKGIKGPQTLRA
255	5752	A	261	3	395	
256	5753	A	262	152	514	LATLLGPWSCARVPSVPALLTPPPL AGPPPPQPLLQRLCSGPRLLLLSLGL SLLLLVDCVIGSQNSQLQEELRGL RETFSNF\TASTEGPSRALSTQGRA MWGRKMEVRLEFPVWRKQQ
257	5754	A	263	138	1072	
258	5755	A	264	1	488	
259	5756	A	265	1	2105	FRAASCAPPSWRMELRSGSVGSQA VARRMDGDSRDGGGGKDATGSED YENLPTSASVSTHMTAGAMAGILE HSVMYPVDSVKTRMQSLSPSSQSPV \PSIYGALKKIMRTEGFWRPLRGVN VMIMGAGPAHAMYFACYENMKRT LNDVFHHQGNHSLANGIAGSMATL LHDVVMNPAEVVKQRLQMYNSQH RSAISCIRTVWRTEGLGAFQESYTT QLTMNIPFQSIHFITYEFLQEQVNPH RTYNPHSHIISGGLAGALAAAATTP LDVCKTLLNTQENVALSLANISGRL



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						VVPMGPLLPNALERGGDGTAHRK AVCGDIREVWELDRLLPCDIRDGAF ITMPFHCYAQNREGELLRPAELAD GAAPRELGGQPGGGPEDGWGQPRW RRRQGPPPGREDYENLPTSASVSTH MTAGAMAGILEHSVMYPVDSVKPR ARPRLLAALRRGRRSGEHRWLRRR LGSRGTRSLKLCTVLPWPFGLAGA AHTCAVSEGVPRRGSPHHAGAEKR VALARPRALGTWCVAAAPRVISGT WGRQVFSRLVAALYRFDSGPWDPL SEGSCCTSSPDFGSPSRREAMTFAFSF CLRGGRHMPSLREHYWARMSHER HKDWANVGGTITVLSEPNFLINNR LARNRTPWARHDNWCHHWQHVS ESSLDCVRLQGLPWMAAAEVEMK LPAGHMHMPVSFPNRSPLGAGCIN
260	5757	A	266	882	1299	
261	5758	A	267	1	2607	MAFAWWPCLILALLSSLAASGFPRS PFRLGvangievystkinksvtsrf AHNVVTMRAVNRADTAKEVSFDV ELPKTAFITNFTLTIDGVTYPGNVKE KEVAKKQYEKAVSQGKTAGLVKA SGRKLEKFTVSVNVAAGSKVTFELT YEELLKRHKGKYEMYLKVQPKQL VKHFEIEVDIFEPQGISMIDAEASFIT NDLLGSALTKSFSGKKGHVSFKPSL DQQRSCPTCTDSSLNGDFTITYDVN RESPGNVQIVNGYFVHFFAPQGLPV VPKNVAFVIDISGSMAGRKLEQTKE ALLRILEDMQEEDYLNILFSGDVST WKEHLVQATPENLQEARFVKSM DKGMTNINDGLLRGISMLNKAREE HRIPERSTSIVIMLTDGDANVGESRP EKIQENVRNAIGGKFPLYNLGFGNN LNYNFLENMALENHGFARRIYEDS DADLQLQGFYEEVANPLLTGVEME YPENAILDLTQNTYQHFDYDGSEIVV AGRLVDEDMNSFKADVKGHGATN DLTFTEEVDMEKEMEKALQERDYIF GNYIERLWAYLTIEQLLEKRKNAH GEEKENLTARALDLSLKYHFVTPLT SMVVTKPEDNEDERAIDKPGAS YQPPQNPYYYVDGDPHFIIQIPEKD DALCFNIDEAPGTVLRLIQDAVTGL TVNGQITGDKRGSPDSKTRKTYFGK LGIANAQMDFQVEVTTEKITCGTG\ RASTFSWLDTVTVTQDGLSMMINR KNMVVSFGDGVTFVVVLHQVWKK HPVHRDFLGFYVVDShRMSAQTHG LLGQFFQPFDFKVS DIRPGSDPTKPD ATLVVKNHQLIVTRGSQKDYRKDA SIGTKVVCWFVHNNGEGLIDGVHT DYIVPNLF
262	5759	A	268	1	1842	
263	5760	A	269	3	377	
264	5761	A	270	1	621	MTKRCLDHRGEWLPAGAGGGGHT GTRCLHHAPVTWVGIEVDIFEPQGI

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						SMLDAEASFITNDLLGSALTKSFSG KKPVWLRGRHTPKGNLDSEVL AGLSPCPIPLAGLTVNGQITGDKRGSPDS KTRKTYFGKLGIANAQMDFQVEVT TEKITLGTG\RA\STFSWLDTVTVTQ DG*APLQGLQGGGLQGEGDHSGPQP NPGALSEPELV
265	5762	A	271	3	2722	FSDGLCMVALSHLGSALQLGSLCFP RSPFRLGKRSLPEGVANGIEVYST KINSKVTSRFAHNVVMTRAVNRAD TAKEVSFDVELPKTAFITNFTLTIDG VTYPGNVKEKEVAKKQYEKAVSQ GKTAGLVKASGRKLEKFTVSVNVA AGSKVTFELTYEELLKRHKGKYEM YLKVQPKQLVKHFEIEVDIFEPQGIS MLDAEASFITNDLLGSALTKSFSGK KGHVSKPSLDQQRSCPTCTDSLNN GDFITITYDVNRESPGNVQIVNGYFV HFFAPQGLPVVPKNVAFVIDISGSM AGRKLEQTKEALLRILEDMEEDY LNFILSGDVSTWKEHLVQATPENL QEARTFVKSMEDKGMTNINDGLLR GISMLNKAREEHRIPERSTSIIVMLT DGDANVGESRPEKIQENVRNAIGG KFPLYNLGFGNNLNYNFLENMALE NHGFARRIYEDSDADLQLQGFYEE VANPLLTGVEMEYPENAILDLTQNT YQHFYDYGSEIVVAGRLVDEDMNSF KADVKGHGATNDLTFTEEVDMEKE MEKALQERDYIFGNIERLWAYLTI EQLLEKRKNAHGEEKENLTARALD LSLKYHFVTPLTSMVVTKPEDNEDE RAIADKPGEDAEATPVSPAMSYLTS YQPPQNPYYYVDGDPH/FSIIQIPEK DDALCFNIDEAPGTVLRLIQDAVTG LTVNGQITG\DKRGSPDSKTRKTYF GKTGASPMAQMGFPGWVTEKIT LLEQARCRAFFSWLDTVTVTQDGH FLASSRRLSMMINRKNMVVSFGDG VTFVVVLHQ/VCWKKHPVPTVDFL GFYVVDSHRMSAQTHGLLGQFFQP FDFKVSDIRPGSDPTKPDATLVVKN HQLIVTRGSQKDYRKDASIGTKVVC WVHNNGEGLIDGVHTDYIVPNLF
266	5763	A	272	1168	1626	RAGRGGEHKLNSYGGRRARSQG HLLSSALSPFVSAASYQPPQNPYYY VDGDPHFIIQIPEKDDALCFNIDEAP GTG\LRLIQDAVTGLTVNGQITGDK RGSPDSKTRKTYFGKLGIANAQMD FQVEVTTEKIT\CGTG\RA\STFSWLD TVTVT
267	5764	A	273	534	690	FVIFSPCSIAMATKENMTSQRGML KSIH\SKMNTL\ANRFPV\NSLIQRV NL
268	5765	A	274	3	946	TTKMAAGTSSYWEGEARRPPDLRK QARQLENELDLKLVFSKLCSTSYSH SSTRDGRDRYSSDTTPLLNGSSQD RMFETMAIEIEQLLARLTGVNDKM

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						AEYTNAGVPSL\NAALMHTLQRH RDILQDYTHEFHKT\KANFMAIRERE NLMGSVRKDIESYKSGSGVNNRRT ELFLKEHDHLRNSDR\LIETISIAMP TKENMTS\QRGMLKSIHKS\MNTLA\ NRFPVNSLIQRINLRKRRDSLILGG VIGICTILLLLYAFHLMGHLQGLLTA TAFTPWSGIRK\HRREKLT\VLISLTS RMNARLTVMDSVTWSG
269	5766	A	275	269	476	VMAVLPSGTALKTNWEPGRDLQOC NGSSLLLSGAPHIVSLLGFIRAKTG RARC\HACNPNTLGGRGGRI
270	5767	A	276	2	424	
271	5768	A	277	3	452	
272	5769	A	278	3	498	PTLLVPTDSERTHHGSCFLPDKTNV KAAVWGKVG\AHAGEYGAELERM FLSFPT\TKTYFP\HFDL\SHG\SAQVK GHG\KKVADALTN\AVAHV\DDMPN \ALSALSDL\HAHKL\RV\DPFNFKLPS H\CLLVTL\AAHLPAEFHPLRW\HALP GTSFLGFL\STVADLPNTR
273	5770	A	279	333	538	IFSSLW\FFILSIKDFILFYFLAQSR SVT\RLECSGTISAHCNLC\LPNSSDF RVLR\LG\NR\LR\KIKK
274	5771	A	280	192	607	GRLWGCVSKKSVGCLPHPGCLWA AFLTLDACGLPSSPWMPVGS\LPHPG CLWAAFLTLDACGLPSSPWMPVTW FPWGLPKLRDPKPPSNLMTRPVSE\P PVLSPSPSPTPSATRPTHFPSLKGA HRPAHVFPFNPCFVP
275	5772	A	281	17	363	GLESEFLLRGLLRPGEQDSALASAV PGSLAQTLPPFW\PLW\TMSFPAHA APHPACCHCLSY\PVSCPVS\PSLLP LGCPLQLLPSCPN\SCYPSPAVPTYCP AGKEEKRRSPSCQACS
276	5773	A	285	96	389	QGPAAENMAAKMF\EFIGKFGLALV DAGGVVNSALYSVDAGHRAVVFD RFRGVQDIVVGKGT\YWLIPWLQKS/ IIFDCRSQPRNV\LVFTGSKDLQIGNL H
277	5774	A	286	1	390	FFYFFFLERDFLFLFYFIFFAVLLLLP NLECNGAISAHRNLR\LPG\SSDSPAS ASQVAGITGMQ\HHAWLSFVFLVKT GFVHLGHAGLKLPTSDDPPTAASDI VGITGMIPPVAGPKQRHFCARSVLV PFI
278	5775	A	287	16	546	QLNGRSIRHEVMSHRKFSAPRHGSL GFLPRKRSSRHRGKVKSFPKDDPSK PVHLTAFLGYKAGMTHIVREVDRP GSKVNKKEVVEA\TIVETPPMVVV GIVGYVETPRGLR\TFKTVFAEHISDE /CRLPLRQKKAHLMEIHVNGGTVA EKLDWARERLEQQVPVNPVFGQDE MIDVI
279	5776	A	288	1	625	CKFIRVMAHTRLRL\LLPLRRKKAHL MEIQVNEGTVAEKLDWARERLEQQ VPVNQVFGQDEMIDVIGVTKGKGY

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						KGVTSRWHTKKLPRKTHRGLRKVA C\KDGLIKNNASTDYDLSDKSINPL GGFVHYGEVTNDFVMLKGCVVGT KKRVLTLRKSLLVQTKRRRALEKIDL KFIDTTSKFGHGRFQTMEEEKKAFM GPLKKDRIAKEEGA
280	5777	A	289	1	903	
281	5778	A	290	38	482	
282	5779	A	291	1	1131	
283	5780	A	292	1	1329	STHASDGVMShrkfsAPRHG\SLGF LPRKRTSRHRGKVKSPKDDPSKVP VHLTAF\LGKAGMTHIVREVDRAP GIHRCNKKERWWRA\THCMRPPP MVGGLVGVYVETPRGPPGPFKT CLLLEH\SDELPRGVFYKEFGH*NL KKKAFTK\YCKEIGKDED\GKKPAW KKDFQQH*KKLLAQVHPCSIAQTQ\ MRLPL\RQK\KAHLMEIQV\NGGT VA\EKL\DWAREKLE\QQVVPVNPSV LGRMRMID\VIGGDQRAKGYKGS PS\RWHTKKAAPAKTH\RG\LRKVG LVLGAWHP\ARVAFSVG\RAAGQK GYPSTALEINK\KIYKIGPGVTLRA GSLIKEQCLHLNYDLSDKSINPLGGF VHYGEVTNDFVMLKGCVVGTKKR VTLRKSLLVQTKRRRALEKIDLF DTTSKFGHGRFQTMEEEKKAFMGPL KKDRIAKEEGA
284	5781	A	293	238	326	HTYKSDTRYERHACWGALL/CNYM RQEC\DSRFVDRPMPVFR\LSVIG TSILYMKAFMHMPFK
285	5782	A	294	2	358	GWGMSLGGAGVEGMEVGTSDLGF FSGQALSPWVSPVPPGLCAWRKD SPVEQKPQGSLPLSALPYLWG/AP WPPAGPQTRGLGPFRGTGSPSPIS RAQKDSWPWPVPSTPACFSAPG
286	5783	C	295	56	175	MASXNRQQFFXNTPXKLLKSPHCNI YRLLSAKSQGKFWK*
287	5784	A	296	1178	1515	KKFMKILEHMFEGFFSFLNFFIFSG GRRSALTARGGSEVAANLGLTCNL HPPGFKRFSLRLRSSWDYRRPPPR PANF\VFSVETGFCYVGQAGLKLT SSDPPASAFPKC
288	5785	A	297	136	251	IHQEKPPNIFSVKKRHYD*PGQHDP LASASQSAGITGV
289	5786	A	298	118	337	IHQEKPPNIFSVKKRHYD*PGQYQK TSLKIQILAGYSGTCLAKSLLRR VGREVIQLALKIRAPIWKIECL
290	5787	A	299	160	437	KRDITTSLGQYQGNP\SLKIQILAG Y\SGTCLAKSQL\RLRLRHQNRNLG GRG\GSEQRSCHLHSWGGHSETVSK KKKKRERQQWRQIGTCMP
291	5788	A	300	61	1302	FSGSCVPPRTCGLCWISTGQSGVVS VSSTRLEESEGTQPPSPSSDTGSEGE EDDEGEEHGLGGQNEVGIIPTTLEFL ENHGKNILLSNGNRTVTRVASYNQ GIVVINQPLVPQLLVQVRIDFLNRQ

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						WTSSLVLGVITCAPERLNFPASACP SNGQPGCCGAVGSSTTSQAGLSSQI CEKFGPNLDTCEPGLTGLRLDSSG GLHLHVNGVDQGVAVPDVPQCH ALVDLYGQCEQVTIVNPEPGAASG KSAGTQGDMEKADMVDGIKESVC WGPPPAASPLKSCYHALCSRFOEL LLLPEDYFMPPPKRSLCYCESCRKL RGDEAHRRRGEPPEYALPFGWCR FNLRVNPRLAAGTLTKKWHMAYH GSNVAAVRRVLDRGELGAGTASILS CRPLKGEPGVGFEEPGTNC
292	5789	A	301	1	936	
293	5790	A	302	1	1023	
294	5791	A	303	1	867	
295	5792	A	304	1	569	SGRVAMGRRRAPAGGSLGRALMR HQTQRSRSHRHTDSWLHTSELNDG YDWGRNLQSVTEQSSLDLFLATA ELAGTEFVAEKLNIKFPAPAEARTGL LSFEESQRIKKLHEENKQFLVVYRG DQTNQNTTPEELKQAEKDNFLEW RRQLVRLEEEQKLILTPFERNLDFW RQLWRVIERSDIVVQIVDA
296	5793	A	306	846	1070	RVGDRSEREIVILKTNTFYQVFPKA GCGCFSFLFSFFLSFFFLRGETESRSV ARMKCSGVISAHCNLCPLGSS
297	5794	A	307	118	340	KFQTEVSHFFLCNLICSYFIFLL/CS FLLIHF/LYSLFFLLFCFMFFLFIMY /LFFVLLIRYSYIKSLLFLMSCN
298	5795	A	308	42	352	TRGPRVPHSGSASSPAQKSGCTG/P* NSALARPALVSFRAMPNSRGW/PQG EQR/PGSPHRSPEGHWKRHVHPPA AQRGPGAGGCHQGTGPEAQGAHQ VRPPAQGG
299	5796	B	309	796	3180	VAEAPGLVDVPGGHPEPQSCEKLE NTGGKIGHRKMPYSTPAPCVSPLK LDLWLSVRERTPDGSLTLLHCATS DPQGGQALCPGGSPQHQLAGQLV VHELFSVLQEICDEVNPLLTLSQP LLGIARNETSAGRASAEFYVQCSL TSEQVRKHLYSGGPEAHSTGIFFV ETQNVRLPETEMWAEPCPSAKGA IILYNRVDVVLASTPMRICPPAAMP LLPLRLCRLWPRNPPSRLGAAAGQ RSRPSTYYELGVLHVGASTEEVKRA FFSKSKELHPDRDPGNPSLHSRFVEL SEAYRVLSREQSRRSYDDQLRSGSP PKSPRTTVHDKSAHQTHSSSWTPPN AQYWSQFHSVRPQGPQLRQQQHK QNKQVLGYCLLLMLAGMGLHYIAF RKVKQMHLNFMDEKDRITAFYNE ARARARSVPALFCSLLPVQEPHFGIP IPTTQAPVSQPDAPGHQRKVVSVID VYTRATCQPREVVVPLTVELMGTV AKQLVPSCVTVQRCGGCCPDGGL CVPTGQHQVRMQVLGTWGNQGG MQILMIRYPSSQLGEMSLSEHSQCE CRPKKKDSAVKPDSPRPLCPRCTQH

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						HQRPDPRTCRCRCRRRSFLRCQGRG LELNPDTCRFSCSLTAGSLLQLTDV WWLLGRLKISLVGEQAQPDHSSHE SQPRCTGRVLSICLSAVATATGAEG KRKLQIGVKKRVDHCPIKSRKGDV LHMHYTGKLEDGTEFDSSLPQNQPF VFSLGTGQVIKGDQGLLMCEGE KRKLVIPSELGGATLVFEVELLKIER RTEL*
300	5797	A	310	61	674	GCGTLGPLQWDFPEPGCKGMMAPL AEGQSSAHISVWGNLRTFCVSTKKI PVDSGASGSPTQVSASLTCSAQAA LDIELGTGLGNNLVSRFGDAKQAG AGLRVKNRAGSPSTRSPEGHWKR VHVPPAAQRGPGGWGLPPRAHGPE AQGAHQVRPPA\QGPQPPAGSGAG RQGSRLWLVRPPVPVGPDPAC HPSRWHPAVAA
301	5798	A	311	89	1166	
302	5799	A	312	1	2094	MGAPAVQSSSGPAGARPRKAGVER RAEPAGPGLPETTRKSPQILGFSLR AVVWDLFPGSKQIVRRKLPIPGQAV LVQADVATLTSRRVLHACGLVPLE MPCIQAYGTPAPSPGPRDHLASDP LTPEFIKPTMDLASPEAAPAAPTALP SFSTFMDGYTGEFDTFLYQLPGTVQ PCSSASSASSTSSSSATSPASASFKF EDFQVYGCYPGPLSGPVDEALSSSG SDYYGSPCSAPSPSTPSFPQPQLSPW DGSFGHFSPSQTYEGLRAWTEQLPK ASGPPQPPAFFSFSPPTGLSPSLAQS PLKLFPSQATHQLGEGESYSMTAF PGLAPTPHLEGSGILDTPVTSTKAR SGAPGG\SEGRCAVCGENASCQHY GVRTCEGCKGFFKRTVQKNAKYIC LANKDCPVDKRRRNRCQFCRFQKC LAVGMVKEVVRTDSLKGRRGRLPS KPKQPPDASPANLLTSLVRAHLDSG PSTAKLDYSKFQELVLPFHGKEDAG DVQQFYDLLSGSLEVIRKWAEEK\IP GFAELSPADQDLLLESFALELFILRL AYRSKPGEGKLIFCSGLVLHRLQCA RGFGDWIDSILAFSRSLHSLLDVDP AFACLSALVLITDRHGLQEPRRVEE LQNRIASCLKEHVA AVAGEPQPASC LSRLLGKLPRLTLCTQGLQRIFYLK LEDLVPPPPHIDKIFMDTLFP
303	5800	A	313	858	1143	QLVPCCPPTQRTVQKNAKYICLAN KDCPVDKRRRNRCQFCRFQKCLAV GMVKEGVWL/RVRPTGARVGLSGV RPPGPPGFCPPGPTGGHVLFPPHL
304	5801	A	314	190	330	ERIKKQDLSICCLQVTHFTFKDSQRL KVKGWKK\IFHTNKNQKRIWT
305	5802	A	315	190	324	ERIKKQDLSICCLQVTHFTFKDSQRL KVKGWKK\IFHTNKNQKRI
306	5803	A	316	85	310	CAWHVNILIGKRLNFTFYRSGTRQG CMLLPFLFNTILKDLVTALKNQDIK GKQIK/EEIKLSLFTEMITRVDKNQS

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307	5804	A	317	33	494	
308	5805	A	318	1	612	
309	5806	A	319	113	551	LLWRESAVTALWGKVNVD\VG GGKALGRLLVVYPWTQRF\FESFGDLST PDAVMGNPKVKAHSKKVLRGAFS GG\LAHL\DNLKGTF\AHTVSLHC\D KL\HVGSWRTFRLLG\NVLVCCCWA HSLLGKEFQPHQLQACLIKKIGWLG VG
310	5807	A	320	221	376	DRVSIPRLESSGAILAHCNFR\SGFK QFSCLSLPSSCDYRCVLPRRALCSSC
311	5808	A	321	32	452	
312	5809	A	322	72	570	SRRAWVSFTEEDKATITSLWGKVN VEDAGGETLGRLLVVYPWTQRF FD SFG\NLTCASAIMGHPKV\VHGKK VLTSLGDA\EHLLDDLKGTFAQLSEL HCDKLHVDPENLKLLGNVLETALAI \HFSAKQFTPEVQASWQKMGD\GV ASALCFTKHLDFMCMMQSFQR
313	5810	A	323	35	359	
314	5811	B	324	102	431	MIIYRDLISHDEMFSDIYKIREIADGL CLEVEGKMVSRTEGNIDDSLIGGNA SAEGPEGEGTESTVITGV\DIVMNH H LQETSFTKEAYKKYIKDYMKSIGK LEEQR\PD*
315	5812	A	325	132	708	RRRRLPSVAIMIIYRDLISHDEMFSDI YKIREIADGL\CLEVEGKMVSRTEG NIDDSLIGG\NASEGPEGEGTRST VITGV\DIVMNHHLA\GNKFSQKEAY KKYIK\DYIEIQFKGETLKEPEDQKR VKPFYDRGLQE\QFKHILG*FSKTYQ FFIG\ENMNP\DG\MVALLDYREGWV *PHI*FSFKD\G\LEMEKC
316	5813	A	326	1	5796	
317	5814	A	327	3	467	
318	5815	A	328	73	1593	
319	5816	A	329	57	1358	RRKVAMDLIPNLAVETWLLAVSL VLLYLYGTRTHGLFKRLGIPGPTPLP LLGNVLSYRQGLWKFDTECYKKYG KMWGTSSLFGPHYPSSYEALGGSC VRLLLCVTP**TRT*GCCVSYN*GT YEGQLPVLAITDPDVIRTVLVKECY SVFTNRRICATTSTIKMQTHSVTMW LPPAVLQSQHGVCLFL*QSLGPVGF MKS AISLAEDDEWKRRSLLSPTFTS GKLKEKRHHKIH\YKMSLTAPCWRK PYPSGT*VCTFNYSIFGAYSMDVITG TSFGVNIDSLNNPQDPFVESTKKFL KFGFLDPLFLSIILFPFLTPVFEALNV SLFPKDTINFLSKSVNRMKKSR\ND LKQK\HRLDFLQLMIDSQNSKETESHK ALSDLELAAQSIIFIFAGYETTSSVLS FTLYELATHPDVQQLQKEIDAVLP NKVRG
320	5817	A	330	870	1150	HRLDFLQLMIDSQNSKETESHKALS DLELAAQSIIFIFAGYETTSSVLSFTL YGTGPLHPDVQAGNCKREIDAVLP

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						NK\APPTYGAVGTDGSYL
321	5818	A	331	144	377	RRCKGISTSCHCIITNEIFIFFEAE SHSV\ARLECSGAVLAHCKLCLPGL RHCPASATREAEAREWLETRSRL Q
322	5819	A	332	3	323	DRVSLSLSPRLECNGMISTHCNLHF PGSSDSPDTP/SQVAEITGVHHHAQL IFVFLVETRFHHIGQAGLELLTSSDL PTSASPSAGIIGVRHCAWARITFQRT KCFSI
323	5820	A	333	187	450	NYVSQKRKKLNSPINY\KEIEFIVLK LPK\KKPLGPNGFTAIFYQTFFKGM \TPILDHLLQKIDVTLPLYFYKTDF LTLKPKTIQKTRA
324	5821	C	334	122	292	MMCSMTLSFIFSMRKLCSIRASS WNSPWFRVSGCPSFTEYWWKVL MVYMLRSS*
325	5822	A	335	295	931	VLSRKCQRSLTAFSSKCPNSWFSITQ TECKTMTCGMPQHVTTQ*RIINTS HQYSVKLGHPHPETRGRFKELVR\ KDLQNFLKKENKNEKVIEHIMEDL DTNADKQLSFR/EEFIMLMGEA*PG AFPRRKIARGLTEGPGVHHKPGPG GGAPPKDHSGPRFTVGHGHGHSTW WPRPQATNHGGQATLPLPNHRPRG LLCQTVLAVGLGAGAK
326	5823	A	336	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
327	5824	A	337	3	556	HSLFGTSEVINKLRSPDAMGHFTEE DKATITSLWGKVNVE\DAGGETLGR LLVVYPWTQRFFDSFGNLSSASAIH GQPPKSRHMGKKVLTSLGDAIKHL\ DDLKGHLLPKPEVNCTCDKAALLD PEELSSFLGEMLLG/VPVFGQSHFRA KEFHPWRLQGFGISRWRQKMVT\ GV\ASALVPSRYH
328	5825	A	338	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
329	5826	A	339	38	547	APSPDAMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF FDSFGNLSSA\SAIMGNPVKVKAHGK KVLTSLGRCHKSTWDDLKG\TFAQ A*SELH\CDK\LVH\DPGGTFKLLGK MLLG*PV\LAIPFSAKEFHP*RLQAS WQKQKMAEDGDLELASALVPSRY H
330	5827	A	340	168	330	SSLGLDLVCGDMAKCTKKVRIISKY GTRYGASLRKMVK\RIAITQHTKYI CSSRA



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331	5828	A	341	2	355	ARATMVLSPADMTNVKAAWGVKVG AHAGEYGAEALERMFLLGTTTKTY FSHFDLSHGSAQVKGHCMKVVDAL TNAGINVDNL\PNAL\DTLIDLLTPIF CRSLNLFYLLISNSLFIIISVH
332	5829	A	342	176	410	AGLLPDP/TITARMNVGVVAHSEVNP NTRVMNSRGIWLAIIILVGLLHMV LLSIPFFSIPGGWTLTNVIHNLATYV FLHT
333	5830	A	343	469	708	
334	5831	A	344	49	351	ATSPD\AMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLDGYPWTQR GFDSFGNLNYTSDVMVDPKFMGHG MKVLTLYLGDALCDLDDTNGNFAH VSTVMC
335	5832	A	345	665	921	AKKKEKKTGALSARRQPNPPTQNT PHPHPPNPTPHHPPPPSPPTPHSPPP FLILQKLLIAVTIFDPTYCVISYSW VIMTFNKL
336	5833	A	346	2	341	HEEGFVNPGARFCLPEAAVRRPPG EATVIMSDQEAKPSTEDLGDKNEGE SIKLP/VLAHSDRTETHFNKTTTHLT SLPQSYCQIQA\PLNSLTLLFARPTT AAHHTPELPMQ
337	5834	A	347	209	397	VSLWQEAMRLPKNTPEEKDRRTAA LQEGLRPVS\PLTLAENGAF\LWS DMENLSDIYWYASE
338	5835	A	348	87	356	IHFYRVKIFFHILCFYIFIQICHYSFIF YFFCRQG/HLSRLEGSGAILAHCNL CLLGSNDPPTSASRVAGTAGTHHH AWLIFVFFIETGY
339	5836	A	349	3	204	KMEARKQRESMRGREAREKEKG YERSSEGERVV\ERNIGHKRRRDAK REARWEKIHGAKEARNRKYK
340	5837	A	350	3	341	HERHEIPIKMSHRGPWLMVDFLSY KLSQNGYSWSQFTDVEENT\TEAPE RTELD\RTTPIAINGNRSWHLADSPA VNGTTGHSSSDARDVIPMAAVQH ALWEASDEFELRHR
341	5838	A	351	67	541	EAPARRALCGRVPSEAQRDGHQAP LLSRRRRL*AFFVADGIFKAELNEFL TRELAEDGYSGVEVRVTPTRTEIIL ATRTONVLGEKGRRIRELTA\VVQK RFGFPEGSVELYAEKVATRGLCAIA QAESLRYKLLGGLAVRRRCAGNQSE DHACLGTNW
342	5839	A	352	3	495	
343	5840	A	353	1	459	EDGYSGVEVRVTPTRTEIILATRTO NVLGEKGRRIRELTA\VVQKRFGFPE GSVELYAEKVATRGLCAIAQAESLR YKLLGGLAVRRACYGVLRVIMESA AKGCEGVVSGKLRGQRANS/MKFG KAGGFPGKLVNYYCALVGPLCAYT GVVGH
344	5841	A	354	1	885	SWSTHASVSAERGGKMAV\QISKK GEFVADGIFKAELNEFLTPQLAED GYSGVEVRVTPTRTEIILATRITQN

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						VLGEKGR\RIRELTAV\VQKRFGFP RRASVELYA\EKVGHYRSCVAIAQG RSLCVYKLLRKGFACAGGPC\YGV AAGSIMEKWGPKAFCVWWSGKT SEEQRA*IP*SFVEWP*WIHSGDPV* LTNVDTAVRHVLLRQG\VLG\IKVK IMLALGTQLGKIGPKKPLPDHV\SIV\ EPKDEIL\PTTPIS\EQKGGKPV TALH GPTRSPQPNRVSLAAVFWSLDVAL
345	5842	A	355	1	284	SLFLYTANSRLGPLVSPAFMPHRISC NVTKGLPHDHYACLQEI KSSYKFYR YFETQQQSV PQCLSRTHQKSRALN NVYSAVRRLQVHMKALLNE*VSPA FMPHRISCNVTKGLPHDHYACLQEI KSSYKFYRYFETQQQSV PQCLSRTH QKSRALNNVYSAVRRLQVHMKAL LNE
346	5843	A	356	1	1404	
347	5844	A	357	1	771	
348	5845	A	358	3	913	
349	5846	C	359	461	667	MRMTMMMMMIHLKLILMMMM KSMEPLLEGAYDPADYEHL PASAEI KELFYISRYTPQLIDL GTTN*
350	5847	A	360	76	158	
351	5848	A	361	1	2313	
352	5849	A	362	788	926	PSPPELPEGDFEGFFPQKLO* SCLPTL QKKKNNNNNNNNNNNNNNNEK
353	5850	A	363	168	447	TGTPGYACNSQNLGGPTGGISRSPV *NQPGQKGETPGFLKIPKLTRGGGR ALQFQVLGRVRPENPLNLGQNFN* PKLCPCSTW GKIRLPF
354	5851	A	364	637	1258	VLFLRKPTPAACLGHALSHRN LGPS AANSPSVLGKPAPSWSHVPATVLP GQQGTPCDMRVSGTVRVGSTVMST TSIPALPHLGSTSVGPPQPGGHEKQ MITWCKDRLQLTHSDEGFGVGFQ TTMYILASKMCTGAQRSGCWALRV PQEDGKNQLIRFYCMYVCIFYETES HSVVQAGVQWRDLDSL*PPSPEFKR ISCLSFLSSW
355	5852	A	365	217	481	KCSFQM*TYRLKNYNNNNHSHPF SISL FLISSNIQNNFGSRYN*NHLKMYKT EAQRLTCSMLHKS NPHLFILNRMFL TRNLLGPHSLVP
356	5853	A	366	1	245	PVPRGGSKLLTHHLAPLTL PKAGDS GVNPRVPPFFLSPPAIWGP KPKILGL AKTPVPRFPLGKKFFPSP*FPPFFPK NKTL
357	5854	A	367	145	196	
358	5855	A	368	120	173	
359	5856	A	369	138	321	NECLLG SFFSV/PNSSLLK*KS*ASA VAHTCNPSTLGG*GGWIT*GQEFET SLANMVKPCLY
360	5857	A	370	1536	1629	KSQKACNPSTLGG*GGWIT* AQEFT TSLANT
361	5858	A	371	11498	11651	LKNNFKKCTMWA\GMVADTCNPST LGGRGGWIT*GQGFKTSLANMMKP

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						CLY
362	5859	A	372	15	272	RLKAATLKMPGSAAKGSEL SERIES FVETLKRCGVPRSED TARVTLLM MRWIFNDHRWIPP*ELVDPYIYFPW PCSTLSCWDWS
363	5860	A	373	433	612	QAPLQKPTVRR*K*VREIRGRD*VE E*IEEWYR*RSGRETRRGRESGR*ER GEVDREERKRE*GSRVRRGRERRG RERRGRERGGEESQEGKREKRKRE RRGREKRGREERKRAKEVFKDGER PRAKVGIVLKRFRQ
364	5861	A	374	785	1178	ALGCPGCPLLAVSGKDHNSSTQPAT HNSRDRRERRKEERERRGRERGEE IEEGKR*RSGRETRRGRESGR*ERGE VDREERKRE*GSRVRRGRERRGR RRGRERGGEERQEGKREKRKRERR GREKRG
365	5862	A	375	1969	2208	GANPIHDLHPHDLTTSRPHIFIFFE MESRSVTQAGVQWHDLSLKSPT GLKLFSLSLPSG*NYRCTPSHLANF CIF
366	5863	A	377	171	442	GKKWSFSLQNWVQAY*LSCNRY CSLKDHDFITPSDGGPDIFLHICDVE GEYVPVEGDEVYKMC SIPPKNEKL QAVEVGITHLGPQTQH
367	5864	A	378	3	775	SVHSSAHASERVAEQNLQGQAMS SVPSPPPQPPTHQA\GVGLLDTPRSR ERSPSPLRGNVVPSPLPTR\TRTFSA TVR\ASQGPVYKGVCKCFCRSKGH GFITPQLMAAPDIFLHISDVEGEYVP \VEGDEVYKMC SIPPKNEKLQA VEVVIT\HLAP\GTKHETWSGHVISF LGDGGSTPCPVLVGRLCGEEAADT GDDILPHETGLQRGNGPSHVSPGGK GYGGAGVGC GFPAISTAYGPLQQ PLHHLKSIKSI
368	5865	A	379	7	316	APSPDAMGHFTEEDKATITSLRGKE NVEDAGG*TLGRLLDDYPWTHRIL DS*GKLLSDYAIMGKQDDKEHA EK ELPSLEDALAHWADASASGHWPSD VPCAYR
369	5866	A	380	61	304	ARTWNSVRMASSGMTRRDPLANK VALVTASTDGIGFAIARRLAQDGAH VVVSSRKSQNVQV*VST*LASV*L IYLMCVLP
370	5867	A	381	2	281	
371	5868	A	382	2	558	HSLLERLRSLISFLVQTPIGHSTEED\ KATI\TSLWGKGEMWKNAGRKKPL GRPPGLSLPQWTPRGSFEQALGNL VSSCPPAPSMGKPPQKSKGTMAKK GA*PSLGKMPIKAPLDDLKGTAFAP A*SELH\CDKLH/VLDPENFKLLGN VLVT\VLAIHFGKEFTPEVQASWQK MVTAVASALSSRYH
372	5869	A	383	3	368	EFFCGLCVKSEISLHLFCLANFFPSL KPQITSSGEMVPLLPCQS*EWRKRD ESSTLPPPPSSGAECPTWLRPSPTS

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						PCPCLPHPYVQGSCLCETQSHLTVNP ASSYRISPPPLISSRTRY
373	5870	A	384	179	455	EFGWGGGKSLGLPRAGLD*IGGSLG FIPLLSTPVSHSHAFSVGAILALIFLL ESLAFQWLLLLSSSHFLYFSLFFRQ SSFCFLTEEQKKKK
374	5871	C	385	22	423	MKAAVLTALXFLTGSQARHFWQ QDEPPQSPWDRVKLHELQEKLSPLG XEMRDXRAPMWTXXNASGPLQRR VRXLWPRALRLSRRTAAQTWPSTT XRPPSILSTFSEKQARVRGTSKA CXPLLESXKGXVS*
375	5872	A	386	1	671	SGRIQEVPHGPFRMKAAVLTAL\VL FLTGSQARHFWQQDEPPQSPWDRV KDLATVYVDGLTEDSGKDSVTSTFS KLRE*LGPVTQ\EFWDNL\EKETEG RQ\MSKDL\EEVKAKVQ\YL\DDF QKKWQEEMELYRQKVEPLRAELQE GARQKLHELQEKLSPLGEEMRDRA RAHVDALRTHLAPYSDELQRQLAA RLEALKENGARLAHYHAKATEHL STLSEK
376	5873	A	388	24	499	HTDTYPHPHLIARPQGFPELKNDTF LRAAWGEETDYTPVWCMRQAGRY LPEFRETRAAQDFFSTCRSPEACCEL TLQVRGPQKRERFMPSVCHLATCL LFPT\PLRRFPLDAAIIFSDILVVPQA LGMEVTMVPKGGPSFPESLREEQDL KRLLDPEMV
377	5874	A	389	109	750	HTDTYPHPHLIARPQGFPELKNDTF LRAAWGEETDYTPVWCMRQAGRY LPEFRETRAAQDFFSTCRSPEACCEL TLQPLRRFPLDAAIIFSDILVVPQAL GMEVTMVPKGGPSFPPEPLREEQDLE RLRDPEVVASELGYVFQAITLTRQR\ LAGRVPLIG\FAGAPWTLMTYMGFI LTWTQNMWAPLWMLCINTHVCFD RTECIPLPSSTTNTDD
378	5875	A	390	1	295	PQTQREPAMVLSPADKTNVKA WGVGAHAGEYGAEALERMILFFT TRTYFRLDLSLSDPV*FPVITEAF ARTYSGVIADLLSNTEPHMIQMAAS
379	5876	A	391	112	310	
380	5877	A	392	49	615	RAQRGCSQSCGKMNARGLGSELKD \SFPVTELSASGPLES\HDLRLKGF\S CVKNELLPSHP\LELS\EFNFQLQPR LK*NFSTLEETFQGSILLPLKITGGDF QGQCRQV\QRLPFSFQAPNLSTGMV FEGGNDETIWDLEDIL**SHHKSEV HGESHTFDGWEYKPWVYCNSAGS WKPRAAILFIVIFVL
381	5878	A	393	167	1955	LCPHVVEGMWEVPVISLMRALIPF MRASPSRVRRRAATPAAVTCQLSNW SEWTDPCFPCQDKK/YTVMTLIAIQT IQGNILISSETLIMSAMAGFPNKYRHR SLLQPNKFGGTICSGDIWDQASCSSS TTCVRQAQCGQDFQCKETGRCLKR

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						HLVCNGDQDCLDGSDEDDCEDVR AIDEDCSQYEPGPSQKAALGYNILT QEDAQSVYDASYGGQCETVYNG EWRELRYDSTCERLYYGDDEKYFR KPYNFLKYHFEALADTGISSEFYDN ANDLLSKVKKDKSDSFGVTIGGPA GSPLLKFIFTRIFTKVQTAHFMRK DDIMLDEGMLQSLMELPDQYNYG MYAKFINDYGTHYITSGSMGGIY ILVIDKAKMESLGITSRDITTCFGGS LGIQYEDKINVGGGLSGDHCKKFG RARKAMAVEDIISRVRGGSSGWSG GLAQRSTITYRSWGRSLKYNPVVI DFEMQPIHEVLRHTSLGPLEAKRQN LRRALDQYLMEFNACRCGPFNNG VPIEGTSCRCQCRLGSLGAACEQT QTE/G*GAKADGSWSCWSSWSVCR AGIQERRRECDNPAPQNGGASCPGR KVQTQAC
382	5879	A	394	94	276	
383	5880	A	395	25	1876	ILQGFACTHLLQFPEYIALFLQGN VRGLLAEMFAVVFILSLMT*QPGV TAQKGNQVRVRPATPAAVTCQLS NWSEWTDGCFCHDKKYRHRNLLQ NKFGGTICSGDIWDQASCSSTTCV RQAQCGQDFQCKETGRCLKRHLVC NGDQDCLDGSDEDDCEDVRAIDED CSQYEPGPSQKAALGYNILTQEDA QSVYDASYGGQCETVYNGEWRE LRYDSTCERLYYGDDEKYFRKPYN FLKYHFEALADTGISSEFYDNANDL LSKVKKDKSDSFGVTIGGPAGSPLL VGVGVSQSQTSLNELNKYNEKK FIFTRIFTKVQTAHFMRKDDIML EGMLQSLMELPDQYNYGMYAKFIN DYGTHYITSGSMGGIYILVIDKA KMESLGITSRDITTCFGGSLGIQYED KINVGGGLSGDHCKKFGGKTERA RKAMAVEDIISRVRGGSSGWSGGL AQRSTITYRSWGRSLKYNPVVIDF EMQPIHEVLRHTSLGPLEAKRQNL RALDQYLMEFNACRCGPFNNGVP ILEGTSCRCQCRLGSLGAACEQTQT EGAKADGSWSCWSSWSVCRAQIE RRRECDNPAPQNGGASCPGRKVQT QAC
384	5881	A	396	2	307	QAGV**WDLGSLQPLPPRLKQFS/CI LNPGNLSKEF*STKETKQNFVGHQ SQTSKFAISLIQHPIPMRSGTKTFM MV*GNKQRSKFPIWTFKIFPDMPLS
385	5882	A	397	374	665	GAQGLSLSPRLECNGAILAHCNLCL PGSSNSPGSAS*VAGTIGMHHLARL MFVFLVESGFHHVGGAGLELLTSSD PPASASQSAGIRGISRRAGLDF
386	5883	A	398	202	425	RLGGVEEGWGKGRSLVLHLKCGV QILLMTLTGKTISL*LDPSDTIVNVK ALIHDIERIPPDHEMLIFACKQLE
387	5884	A	399	202	418	RLGGVEEGWGKGRLLNLRLRGGL

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						HIYMITILDLNISLEDMPNPTI*NVK AMILSNNGIHSHE*RLIFEGMR
388	5885	A	400	144	433	
389	5886	A	401	1	3135	
390	5887	A	402	79	929	PVAQGMLRWTVHLEGGPRRVNHA AVAVGHRVVSFGGYCSGEDYETLR QIDVHIFNAVSLRWTKLPPVAPGEV CHPWASS\VPYMRYGHSV\PSDD TVLLWGGRNDE\GPCNVLYAFDV NTHKWFTPRVSGTVPSARDGHSAC VLRKIMYILGGYEQQADWFSNDIH KL
391	5888	A	403	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSFGNLSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
392	5889	A	404	50	562	APSPDAMG\HFTTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF DFSFGNLSASAIMGNPKVKAHGK KVLTSLGDAI\EHLDDLKGTFAQLSE LHCDKLHVDPENLKLGNVLETAL AIHFGAKILPFKGRLPGRRWQKMV TGVASALCFTKHLDFMCMMSQSFQR
393	5890	A	405	228	420	TPEADALYSHNPGGNLDRHTASKPS ALLQGPAPWQRGSACSLQILPESRV GFPTGPP*ARKVSI
394	5891	A	406	653	940	KWKKINVFFETGSRSAQARVQWC HLGSLQP*HPRLKEPPASASQTAGT TGMHHHAWLS*VSFVKMRLGHIIQ DIRRLMDSINMPHYMHQAPPMCO
395	5892	A	407	795	1802	CRLHTQQIQRLETASGFLRMKGKNS VQLQEGWERFQDPGNHITRPRPFLP SDPHPTLMCLQGPPPTGKGPGKSRAT GTAAEGA\DETSYF*NAFQLPLYK LIKIRKKEK*K*KSCT*KRVRWSKL CPRDWAAARTEAPPTGLESRQPVC Q\DPPLPTAACIPP/CWLGSF*KRM ND*QTKITPWG*FPHHPRL/PPSSSPS NSSSPSSPSKLSSSMASPVKYST ARGTIRSRKKCPISKSEANVNSESSS SDSPSPDATDLPFNGLKKLKKDSL TCFVIVLTVPRPLCFCCFLMVLTVTF FPFFQSIVHPSQSTISGPSKEKGSALS GSDFIL
396	5893	A	408	342	515	
397	5894	A	409	3	333	AAWLLLGAATGLTRGPA/PRPSPPR ALTPA*GPLAAFTAARSDAGIRAMC SEILRQEVLDKDFHRDLLIKVKFGE SIEDLHTCRLLIKQDIPAGLYVDPYE LASLRERNITEEKTSWRRLWLPSDN
398	5895	A	410	877	1206	QGGQSSLGTAGPEPDSPGDPGSAAE QSAREGRRAHGSNV*PPPARSTD LG PAPGPHIPATREAREPGPLPRSGPP SPAPLTGVRARGGEGRGPPAREPG RRPEEQPGR

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399	5896	A	411	238	326	LHSGPGVVVT*YRKMTSLWAGCSR HACNPSTLGSRGIQITRGQEF
400	5897	C	412	194	474	MWKMHMCMERHGSTVLAIYLRQQ MPQHFFSHSSQYIHILANENYLGSLP FLLKHKFFIKCCIPASSNAHADFR ARRKETAAPQPCRRPAAR*
401	5898	A	413	1	88	
402	5899	A	414	65	191	
403	5900	A	415	131	363	EVKMAGFLDNFRWPECECIDWSE RNVVASVVAGILVSEKDWLVTCIPY LLPWKLMPVPLN*EWLSRTIYFTAV LYR
404	5901	A	416	146	567	EVKMAGFLDNFRWPECECIDWSE RNAVASVVAGILFFTGWWMIDAA VV\YPKPEQLNHAFTCGVFSTLAF FMINAVSKLLQVRGDSYGKAAVL GRTGA\RVWAFHWGFMMLMFGSLIA SMWILFGAYVTPKYLFI
405	5902	A	417	17	369	KLTFGLGLGVPPKPVIPFKNRPIGP PWVPPVIPAPLEAQVGGSPSPEIGAP PGYKGEPPFFLKPKQKFTRCQGPPL SQVPWSFRPKKGLNPGSRAFH*LRS RPCPSTWATKPNFVS
406	5903	A	418	553	673	RRIKGGVQWLTPVISVLWEAAAG D*LEASSRLYATPPD
407	5904	A	419	2	427	HVIKVLHDDWIFTPIQGP*SM/CSS KNESRHIGS*RTVG*LLEVLSLL*S FGRLNALNMKSL/TSEVQEE*RKLN KTHRVQRDFDKDRKLAVGQSESPG HPTSEKPPSTSSAGCMLCSLHISRG FQLRRKRQLNGKCCPIQ
408	5905	A	420	82	371	RRHSVACTPHPSSQVLKSL*SFGRL NALNMKSLKAKFRKSDVN*IKLIEC KEPSTEN*LLARVKVLVIRLPRNLL QPHRLLAVCYAAAYISPLAFS
409	5906	A	421	103	430	SFGRLNALNMKSLKAKFRKSDTNE WNKNDDRLLQAVENGDAEKVASL LGKKGASATKHDSEGKTAFLHAAA KGHVECLRMITHGVDVTAQDTTG \HSALHLAAKNSHHE
410	5907	A	422	87	283	SFGRLNALNMKSLKAKFMKSDTNE WNKNDDRLLQAV*NGDAEKVASL LGKKGASATKHDSEGKTA
411	5908	A	423	2	424	
412	5909	B	424	108	395	VGAHAGEYGAEALERMFLSFPTTR TYFPHFDLSHGFCPLRGHGKEGGR RADQRRGQRGTTCPTSLSALSDLHA HKLSSGTRFNFQAPKATGLLG*
413	5910	A	425	2	334	
414	5911	A	426	236	649	
415	5912	A	427	76	322	TNSPCYVVFNGNSFFS*IENKKQENK VQQAGIRLYGALLTKCPRLYSKQIH PALLRRLQHGVDLVYFEDILDKLIG HGPGSV
416	5913	A	428	988	1223	RGERADHLRSGIRDQPGQHGETPSL LITQKLAGLGSACL*SOLLGRLRQE NCLNAGVGGCSEP*SRHCTPAWAT

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						ERDS
417	5914	A	429	57	349	ERESPFAPRLEGKGANLG*WKAPLP GLSPFSGLSLPRTGNYGPPQPPVNF F*F*GETGFPRLTREGNLRPSENPA LVKPQNKVAPKHGVEKPGGK
418	5915	A	430	291	594	SWLFRLGAMAHAYNNSSLGGQSGR IVWAQEFNTQPGQHRGDPLYK*FF FLISQCDGMHLWSQLRLRLRQKDH LNPRAQGCSEL*LHCCAPAWVTEQ DLSQ
419	5916	A	431	27	361	RGPTVTPQIMAVEDVASTGADPCD LDSGLLHEILTSPLLLLLGLCIFLL YLIVR*DQPAANGSDDDD*PSPLPR LKRRDFTPDLLRRFYSVQDPRILMD FNCKVFDVTK
420	5917	A	432	196	555	SPSMNPRKKVDLKLIVGAIGVGKT SLLHQYVHKTFYEEYQTTLGASILS KN*SYWVDTTLKVTDLGDGTGGQER FRSMVSTFYKGS DGCILTFDVTDL SFEALEFWPGGGLAQNGPNEA
421	5918	A	433	1	685	EIKYHSLPRLECRGEISAH*NLCPLG SSDSPATAS*VAGITGMRHYAQLIFL FLVET*FHHVGQGWSTPDSNDPPA SASQGAGDYRRD
422	5919	A	434	56	335	KCSPKILLTSESTSSNPCLIDTNASDF HFLSQVLE*VVSPKGSKEALCCILR HLGYETRESCPWCP SQFRYITFDMG SYVGPVLHHSCQALSL
423	5920	C	435	24	332	MKGRTFISLLFLFSSAYS RGVFRRD AHKSEVAHRFNDLGEENFRALVLIA FAQYLQQRPFEDHVTYYAQLQLFV KPMVKWLTA VQNKNLREMNASCN TXMTTH*
424	5921	A	436	130	599	
425	5922	A	437	1	404	
426	5923	A	438	3	647	FSLSTPHAFGTMKWVTFISLLFLFS SAYS RGVFRRDAHKSEVAHRFKDL GEENFKALVLIAFAQYLQQCPFEDH VKLVNEVTEFAKTCVADESAENC KSLHTLFGDKLCTVATLRETYGEM ADCFLQHKDDNPNLPRLVRPEVDV MCTAFHDNEETFLKKYLYEIARRHP YFYAPELLFFAKRYKAAFTECCQA ADKAACLLPKLDEL RDEG
427	5924	A	439	323	899	MMRVFLSEKALSSSYLEMYLSTPH AFGTMKWVTFISLLFLFSSAYS RGV FRRDAHKSEVAHRFKDLGEENFKA LVLIAFAQYLQQCPFEDHVKLVNE\ AKQEPERNECFQHKDDNPNLPRL VRPEVDVMCTAFHDNEETFLKKYL YEIARRHPYFYAPELLFFAKRYKAA FTECCQAADKAACLLPKLDEL R
428	5925	A	440	1	1206	SFSLSTPHAFGTMKWVTFISLLFLF SSAYS RGVFRRDAHKSEVAHRFKD LGEENFKALVLIAFAQYLQQCPFED HVKLVNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGE



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						MADCCAKQEPGRNECFLQHKDDNP NLPRLVRPEVDVMCTAFHDNEETF LKKYLYEIARRHPYFYAPELLFFAK RYKAAFTECCQAADKAACLLPKLD ELRDEGKASSAKQRLKASLQK/PR NLGKVGSKCKHPEAKRMPCAEDY LSVVLNQLCVLHEKTPVSDRVTKC CTESLVNRRPCFSALEVDETYVPKE FNAETFTFHADICTLSEKERQIKKQT ALVELVKHKPKATKEQLKAVMDD FAAFVEKCKADDKETCFAEEGKK LVAASQAALGL
429	5926	A	441	28	1587	
430	5927	A	442	1	1652	GTMKWVTFISLLFLFSSAYSRGVFR RDAHKSEVAHRFKDLGEENFKALV LIAFAQYLQQCPLEDHVKLVN\KDD NPNLRLVRPEVDVMCTAFHDNEE TFLKKYLYEIARRHPYFYAPELLFF AKRYKAAFTECCQAADKAACLLPK LDELDEGKASSAKQRLKASLQK FGERAFKAWAVARLSQRFPAEFA EVSKLVTDLTKVHTECCHGDLLEC ADDRADLAKYICENQDSISSKLEK CEKPLLEKSHCIAEVENDEMPADLP SLAADFVESKDVCKNYAEAKDVFL GMFLYEYARRHPDYSVLLRLAK TYETTLKCCAAADPHECYAKVFD EFKPLVEEPQNLKQNCLEFEQLGE YKFQNALLVRYTKKVPQVSTPTLV EVSRLGKVGSKCKHPEAKRMP AEDYLSVVLNQLCVLHEKTPVSDR VTKCCTESLVNRRPCFSALEVDETY VPKEFNAETFTFHADICTLSEKERQI KKQTALVELVKHKPKATKEQLKAV MDDFAAFVEKCKADDKETCFAEE GKKLVAAASQAALGL
431	5928	A	443	1	1515	MKWVTFISLLFLFSSAYSRGVFRD AHKSEVAHRFKDLGEENFKALVLIA FAQYLQQCPFEDHVKLVNEVTEFA KTCVADESAENCDKSLHTLFGDKL CTVATLRETYGEMADCCAKQEPER NECFLQHKDDNP NLPRLVRPEVDV MC/H/YPNAAQNPW* TGDHAFQLW KSMKHFTFPKSLMLKHSPSMQIYAH FLRRRDKSRNKLHLLSL*NTSPRQQ KSN*KLLWMISQLL* RSAARLTIRRP ALPRRVKNLLLQVKLP* AYSRGVFR RDAHKSEVAHRFKDLGEENFKALV LIAFAQYLQQCPFEDHVKLVNEVTE FAKTCVADESAENCDKSLHTLFGD KLCTVATLRETYGEMADCCAKQEP ERNECFLQHKDDNP NLPRLVRPEV DVMCTTKCTESLVNRRPCFSALEV DETYVPKEFNAETFTFHADICTLSE KERQIKKQTALVELVKHKPKATKE QLKAVMDDFAAFVEKCKADDKE TCFAEEGKKLVAAASQAALGLTCEA CQEPGGLVVPPTDAPVSPTTLYVED

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						ISEPPLHDFYCSRLLDLVFLLDGSSRLSEAEFEVLKAFVVDMMERLRISQKWVRVAVVEYHDGSHAYIGLKDRKRPELRRIASQVKYAGSQVASTSEVLKYTLFQIFSKIDRPEASRIALLMASQEPQRMSRNFVRYVQGLKKKKVIVIPVGIGPHANLKQIRLIEKQAPENKAFVLSSVDELEQQRDEIVSYLCDLAPEAPPTLPPDMAQV
432	5929	A	444	2	1848	RFSLLSTPHAFGTMKWVTFISLLFLFSSAYSRGVFRDRAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKS LHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNP NLPRLVRPEVDVMCTAFHDNEETF LKKYLYEIARRHPYFYAPELLFFAKRYKAAFTE\CCQAADKAACLLPKLDELRE*LNQKHVLLMSQLKIVTNHFIPFLETNYAQLQLFVKPMVKWLTA VQNKNLREMNASCNTKMTTQTSPDW*DQRLM*CALLFMTMKRHF*KNTYMKLPEDILTFMPRNSFSLKGIKLLQNVAKLLIKLPACCPKLDEL RDEG KASSAKQRLK CASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLT KVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSV VLLLRLAKTYETTLEKCCAAADPHECYAKVDFEFKPLVEEPQNLIKQNC ELF EQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKLPSC**SC\CLLPKLDEL RDEGKASSAKQRLK CASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLT KVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSV VLLLRLAKTYETTLEKCCAAADPHECYAKVDFEFKPLVEEPQNLIKQNC ELF EQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKLPSC
433	5930	A	445	1	3780	MKWVTFISLLFLFSSAYSRGVFRDRAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENC DKS LHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQH/KCFLQHKDDNP NLPRLVRPEVDVMCTAFHDNEETF LKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDEL RDEGKASSAKQRLK CASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLT KVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLEK

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						SHCIAEVENDEMPADLPSLAADFVE SKDVCKNYAEAKDVLGMFLYEY ARRHPDYSVLLRLAKTYETTLEK CCAAADPHECYAKVFDEFKPLVEE PQNLIKQNCLEFEQLGEYKFQNALL VRYTKKVPQVSTPTLVEVSRNLGK VGSCKCKHPEAKRMPCAEDYLSVV LNQLCVLHEKTPVSDRVTKCCTESL VNRRPCFSALEVDETYVPKEFNAET FTFHADICTLSEKERQIKKQTALVEL VKHKPKATKEQLKAVMDDFAAFV EKCKKADDKETCFAEEGKKLVAAAS QAALGLTPLGPASSLPQSFLKCLE QVRKIQGDGAALQEKLCAATYKLCH PEELVLLGHSGLGPWAPLSSCPSQAL QLAGCLSQLHSGFLYQGLLQALE GISPELGPTLDTLQLDVADFATTIW QQMEELGMAPALQPTQGAMPAFAS AFQRRAGGVLVASHLQSFLEVSYSR VLRHLAQ
434	5931	A	446	2	2255	STPHAFGMTKWVTFISLLFLFSSAYS RGVFRDAHKSEVAHRFKDLGEEN FKALVLIAFAQYLQQCPFEDHVKL NEVTEFAKTCVADESAENCDKSLH TLFGDKLCTVATLRETYGEMADCC AKQEPERNECGTMKWVTFISLLFLF SSAYSRGVFRDAHKSEVAHRFKD LGEENFKALVLIAFAQYLQQCPFED HVKLNEVTEFAKTCVADESAENC DKSLHTLFGDKLCTVATLRETYGE MADCCAKQEPERNES/CFCNHKKD NPNLPRLWRPEVDVMCTAFHDNE ETVFLKKYLYENCPPERHPLPFMAPG NSFSF\AKRYKAAFTECC\QAADKA ACL/LCPKLDELRG*KGRLRSKQR LKASLQKFGERAFAKAWAVARLSQ RFPKAFAEVSCLVTDLTKVHTECC HGDLLCADDRADLAKYICENQDSI SSKLKECCEKPLLEKSHCIAEVEND EMPADLPSLAADFVESKDVCKNYA EAKDVLGMFLYEYARRHPDYSVV LLRLAKTYETTLEKCCAAADPHEC YAKVFDEFKPLVEEPQNLIKQNCLE FEQLGEYKFQNALLVRYTKKVPQV STPTLVEVSRNLGKVGSCKCKHPG AKRMPCAEDYLSVVLNQLCVLHEK TPVSDRVTKCCTESLVNRRPCFSAL EVDETYVPKEFNAETFTFHADICTL SEKERQIKKQTALVELVKHKPKAT KEQLKAVMDDFAAFVEKCKKADD KETCFAEEGKKLVAAASQAALGL
435	5932	A	447	1	477	FYNRVLLLLPRLEC*GVIFPHRNHL PGSSDSHALAFRVTGITGTCHHACLI FVLLVETRFLHVGQAGLELLTSSDP PSSASQSSGITGVGHCAGPTAHFLP HKVLRSLSTKLPSGMSPETIHPRRHA EKSCLFSFSLYLFHLTSSCSFIHPFSIL TFKC

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436	5933	C	448	141	390	MAKFSLCPPVKERGEKAHWEXXX XXNKATNSICEVSTFMXXXXXXXXXX XXXXXXXXXXLNIHYESDWVISKLIP GCIKMTEAITC*
437	5934	A	450	345	462	NQRSTARGKELLQDTRALKKNS*R VIKYSKQQAQTCEG
438	5935	A	451	1538	1709	SKCKLKQDP SHAGTSLQSLLRRLR QENPLRPGFQGCSEL*SYHCTPARV TEQDPIS
439	5936	A	452	243	353	YSYHIRVHVHTPHLHACP*LHTVR YT*NSTHTHTYF
440	5937	A	453	2	366	SLPASDRPPISSPLATSGTIFSAISCF WDLPAFLWLAPSCQPTMSSQIRQN YSTDVEAAVNSLVNLYLQASYTYL S\LQDIKKPAEDEWGKTPDAMKAA MALEKKLNQALLDLHALGSART
441	5938	A	454	2	797	LIGKFAPRGPRJRQRRGGPARVWSL CFKQVFGTEQDPGILFPASGPPSDFL LRLQTS GTIFSAISCF LGPAQHRFLW LAPSCQPTMSSQIRQ\NYSTDVEAA VNSLVNLYLQASYTYLSLGFYFDR\ DDVALEGVSHFFRELAEE\KRKGYE RLK\MQNQ\RGG\RALFQDIKKPA EDE\WGKTPD\AMKAA\MALEKKLN QAL/LWDLHALG\SARTDPHLCDFL ETHFLDEEVKLIKMGDHLTNLHR LGGPEAGLGEYLFERLTLKHD
442	5939	A	455	2	331	FFVFCFGKRGGLAVFRVEGKGMNPG *RNLWLPGLKNFSGTLWRGGNNK PGPPLQPKFGFLKKKGFSPPGQGGF KIPNLEIGPNKGPKGWE*RA*PPNPS PSNFFNKPWVG
443	5940	A	456	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMTGVASALSSRYH
444	5941	A	457	38	533	APSPDA\MGHFTEEDKATIT\SLWGK VNVE\ DAGGETLGRLLVVYPWTQR FFDSFGNLSSASAI\MGNPKVKAHG KKVLT\SLGDAIK\HLDLKGTFQAQ A*SEPAPVTKLHVDPENFKAPGEM LLVTR/VLAIPFSAKEFHP*RLQASW AE/MMGDLQLASALVPSRYH
445	5942	A	460	3	198	GIPGSSFCGLCGDVP GKPV*RADGS C*DG VAPRLLRPRGFRGRCGPVLD SLAGQRGAESGCRG
446	5943	A	461	649	1185	ETCLAFMYQRTCSADSKRYIWQLF LEKGPMGYHPLHF*VFLGFFFFFFFET VLAVLPQAGSVGGHNHSSIASNNHP RA*ANPPHLVAGDYKLTAQPGLKF/ VFLLETGFSYVCPGWVSGSLGSNGP PAPAFQRHRAKFVSFVPCHHAAQK GSIPFNELTFINWVMLGGASSLSWEI VNSS
447	5944	A	462	1	298	NKEILARPNGSSPEFPPLWGLRQVD

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						PPESGVQSPASPHGKTLFLLKKPTLT GQGGPNPVFPVLRVVKPQGPNPG GGGFH*PKSCPCPEWGAKLDPVF
448	5945	A	463	179	351	RHVGKIHGDHEATEKFIDEFAKVIA DKHLTLEQVYNANETSLF*HYYPR KTPITAAE
449	5946	A	464	1	327	PGVPMQRAEFEQPYKRSRCDDSPRT PSNTPSAEADWAPGLELHPDYKTW GPEHGCSFLRRGGFDKPVLLKNIRE NEITGALLACPDSESFENLGVSVLR* T*KLLNYYYS
450	5947	A	465	261	452	GDLRVTGAPSVLSLSP*LGLP*VSRP* VPSPLASGTSKPLARFPEEAVGFSSRP GLCLLSIFPGL
451	5948	A	466	362	991	PSRHLSWLWGSTGCRNAHVQLAG GAGARAGEERPCFPRPELAGTVSPG DKSLRQFGEKGGGGHERMQGPHHS SKESGGQSHGEDPSLEASPPKPESPA SQVPMKSPPVIPGETAHGLP*VSRP* VPSPLASGTSKPLARFPEEAVGFSSRP GLWSAMQAGVCDQGICAIRNSPQT TQGGRRP*ERRCRYMHVTTEKAAF TPSAPRECLPH
452	5949	A	467	24	436	RFIVLVHYISAPGELCRGWGSPKME GWGKRTSCQSLPKAGRSPGSLSRD EYCGHRLPDNV*ATGGGQGPAPG MGVRNPSPAPRTSPGWRVPSNTAP QLLGCFGGQTGRVPFIQDPDSSSSG MRNSPPGRGCLESA
453	5950	A	468	2	424	
454	5951	A	469	3	452	
455	5952	A	470	2	467	PDSSGPHRLRENPPWCLSPADKTNV KAAWGKVGAVHGEYGAELERMF LSFPTTKTYFPHFDLSHGSAQV\KGH G\KKVADALTNVAHVDDMPNALS ALSDLHAHKLRVDPVNFKLL\SHCL LVTL\AAHLPAEFTPCGGTASLADKF LGFLKQRC
456	5953	A	471	61	346	VRARVPSPAAAMGCTLSAEDKAAV ERNKKIDRNLREDREKAAKEVKLL VLGAGESGKSAIGKPMIIEEGYIQ DEWKPFKGIVYSNTLQAIIGT*KAA VERNKKIDRNLREDREKAAKEVKL LVLGAGESGKSAIGKPMIIEEGYI QDEWKPFKGIVYSNTLQAIIGT
457	5954	A	472	828	1066	QAQWLTPCNAQHFAPRRANHLRL GV*HQTGQHGTSPSLKKEYKKKK KVASRSHMSVIPTMWKAEAQELLE PGRQRSQ
458	5955	A	473	180	350	EPMAKGKTESPGPKRCGP*I*WVIS QRGTLRFRGAGLFFMGEFLRLGENL LEIPRGA
459	5956	A	474	1689	1856	GRCHITCVKSHGAADFDTTFILFY FILFYFILFIF*TESCSVTQAGVQRGN LGSL
460	5957	A	475	115	324	SNFQLSRKLYF*FFQGKSKHNEYFII FE*T*ILHFLNLGIVIYNYGTSFRKNR

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						MKRK W V N D K M G Q Q Q K H G
461	5958	A	476	310	633	R F S L G E Q E C E V C Y R L R P T P G W T P G E T A G V A G R E P L V C S P P P P P A S P C A P P K V R S D M G P Q C P C A S * W P S G L T K G P S C P F P V A S H G G I T P G Q W P G E E T S R K E R S S A T K
462	5959	A	477	2	293	P A A E R S C L R V T F A S A C P A S M E P K R I R E G Y L V K K G S V F N T W K P M W V V L I E D G I E L Y K K N C D N S P * G M I P L R G I T L T R P W L D F G R R K C W F T K S S I Y Q Y L
463	5960	A	478	387	511	W D I P I F I S D I Y I I L I T G Y L T T Y * N V L H W K K I I Y F Y I A L I V L
464	5961	A	479	130	240	K N E Q D P R D L * D N D K W P N I H V I G V P E E D K D N G T E R V F D
465	5962	A	480	116	423	G I R C P G P R E A S L L S Q F I L S M R Q A G Q D W Q P E A Y T L R I C Q L E V F S T C V S S L L H P V C R S Q * L P M E P E V I P G W N G K P R G H W P V Q I F K S F T H G T P N L A G P G C C C G V R
466	5963	A	481	64	343	Q L L * * L S S T W E G L Q A A K E L D E Q R G I G C
467	5964	A	482	61	342	Q P Q T D T M G H L T P E E K S A V T D L W G K V N A D E A D G E A L V T L L G V Y P W T Q R M F E S F G D L D T P E A D M G N P K V K A H G W K V L * A F I D G P A H P D Q L K G N L C T
468	5965	A	483	557	816	S R H F E R P W V D H L R L G V * D Q P G Q H G E T P S L Q K I Q K L A R S G G T H L * S S Y L G G * S G K N H L N P G S Q G C S E P * S C H C T P G W V T E Q N S V S K K
469	5966	A	485	277	322	F F F * V Y H V W F L F S F L I C R F M P F A K F G N F * P L F L E I F F H P Y S F S S L * Y E W * S F C Y C L R G L L C F H V Y P L F L V Y F S L F F I L V N F C * L F F S S L I L F F C H M Q S T V E L V Q
470	5967	A	486	31	309	F L E L G P G K P F G N M Y D A D D D M Q Y D E D D D E I T P D L L Q E T C W I V I R S Y F D K K G * V I Q Q L D S F D * S I H M T A L R I G E Y A A P I D L Q A D A H H A S G E G E K P
471	5968	A	487	130	521	K A K F R T F C T S S F Y N * D L D F K I Y P S P I K V A E P S * L S G Q C F S S L F F H Q D L G F C F V L L F E T E S C S V T Q V E H S G A I S A H C N L R L P G * S N S P V S V S L A A G T T G T H H Y T Q L I F V L V A E M G F C H V G Q S G L E L A S C R
472	5969	A	488	32	452	
473	5970	A	489	38	525	A P S P D A M G H F T E E D K A T I T S L W G K V N V E D A G G E T L G R L L V V Y P W T Q R F F D S F G N L S S A S A I M G N P K V K A H G K K V L T S L G D A I K H L D D L K G T F A Q L A S E L H C D K L H V D P E N F K L L G N V L V T V L A I H F G Q R I H P * R C R A S W A E D G * L G V A S A L V L Q D T T E L T C P
474	5971	A	490	818	947	V C F L F L F F * D G V S L M L P R L E C N G T I S A H R N L C F P G S S D S P V S A
475	5972	A	491	17	416	P P S S N P M G H F T * E D T A T I T S L W G T V N A E N A G G K T L L R L L G A Y P W T Q R L F D S F G N L S S A S A I M G N P Q G K A H G L K V L T L L * D A V K H L D D L M G T F S H P T E L

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						PCYKLHLDSENKLLGYVLAIVMAI HFGKEVIPAV
476	5973	A	492	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRRFFDSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
477	5974	A	493	34	548	APSPDA\MGHFTEEDKATITSLWGK\ VNVE\DAGGETLGRLLVVYPWTQR FFDSFGNLSSASAI\MGNPKVKAHG KKVLTSLGDAIKHLDDLKGTFAQL\ SELH\CDK\LHVDPENFKLLG/NMLL VTRFGQSHFRAKNFTPEGCRASWQ KQKMAEDGDLQWPVPCSSRIPLKP LGP
478	5975	A	494	527	1022	GWASAFWLIIKPGSPRGYRCNPHH VILPVSAGLELPLCSLLPSTDTCPAS QTGSGRANRATPGCGRPAGVRKGR PACKRSKNFRAACGSGARSRPGRH TPGSSRPPGRQKRAPWASQARRPPA *SRPGGRGGAARPHPRRTGAPAGSA RGAQRSERARPQPRDPA
479	5976	A	495	2	379	
480	5977	A	496	3	723	VPRVCLLLQQCLDGTDPGTGLPASD RPPISSPLATSGTIFSAISCFWDLPA FLWLAPSCQPTMSSQIRQNYSTDVE AAVNSLVNLYLQASYTYLSLGFYF DRDDVALEGVSHFFRELAEEK\REG YERLLARMQNQ\RGGRALFQDIKKP AEDEWGKTPDAMKAAMALEKKLN QALLDLHALGSARTDPHLCDFLETH FLDEEVKLIKMGDHLTNLHRLGG PEAGLGEYLFERLTLKHD
481	5978	A	497	1	196	GTSVTKMEAFILGSRSLWAGGPAP GQFYRITFTPDSFMDPASALYRGPIT RTQNPMVTGTSVLGV*IEGGWVIA GHMLGFYVCLDRDRFYRFRVNL STVLDASGDAE*HYL*QFYRITFTP DSFMDPASALYRGPITRTQNPMVTG TSVLGV
482	5979	A	498	1	401	GTRKWVTFISLLFLSSAYSARGVFR RDAHKSEVAHRFKDLG*ENFKALV VIAFAQYLQQCFEDHVKLNVNTE FAKTCVADESPDN*D*SLHTLFGDK LCTVAILPETYGEMADCCVQLEPER NECFLQLKD
483	5980	A	499	47	411	
484	5981	A	500	316	493	LLVGRALPEGDRHDQHQQGLEQS ILKLEKEIQDLENAELQISTKEEAIL* KLKAIER
485	5982	A	501	27	526	LSLTSRMEEAELVKGRQAITDKRK IQEEISQKRLKIEEDKLKHQHLKKK ALREKWLLDGISSGKEQEEMKKQN Q\QDQHQIQVLEQSILRLEKEIQDLE KAELQISTKEEAILKKLSIERTTEDI IRSVKVEREERAEEESIEDIYANIPDLP

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						KSYIPSRLRKEIN
486	5983	A	502	25	208	VSRIEAVSGSHGFSIHKLLTVNVITY DCVSSWCLYVSFQQKDPLVLGQRQ LKSKPAGDLNT*GKVIKCKAAIAW KAGKPLCIEEVEVALPKAHEARIQV SRWFRLELSLA
487	5984	A	503	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGEKFTF EVQASWQKMTGTVASALSSRYH
488	5985	A	504	52	562	APSPDAMGHFT*EDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF FDSFGNLSSASAIMGNPKVKAHGK KVLTS LGDAI\KHLDDLKGTFAQLS ELHCDKLHVDPENFKLLGNVLVTV LAIHF\GEKFTPEVQASWQKMAED\ VTGVASALCFTKHLDFMCMMSFSQ R
489	5986	A	505	801	927	
490	5987	A	506	659	837	RKIKEAGHRGSQLYSQHFGRLRQE DCLSPGGQGCSEPRLRHRCVPAWVT G*KKTLPKNKQ
491	5988	A	507	3	203	
492	5989	A	508	23	678	RPRVRMAEVQVLVLDGR\GHL\LR LAA/LSVAKQVLLGRKVVVRCEGI NISGNFYRNKLKYLAFLRKRMTN PSRGPYNFRAPSRIFWRTVRGMLP HKTKRGQAALD\RLKVFDGMPPPY D/KAPLFL*QKKRMVVPAALKVVR LKPTRKFAYLGRLA\DEVGWKYQA VTAT\LEEKREKAK\IHYRKKK*L\ MRLRKQ\AERNVRRIFANTPEVLKT HGLLV
493	5990	C	509	275	370	MPQGGACSPVLPGLVVSLLLTQSY LVVVPQW*
494	5991	B	510	1	1122	MVFLSGNASDSSNCTQPPAPVNISK AILLGVILGGLILFGVLGNILVILSVA CHRHLSVTHYYIVNLAVADLLLT TVLPFSAIFEVLGYWAFGRVFCNIW AAVDVLCCTASIMGLCIISIDRYIGV SYPLRYPTIVTQRRGLMALLCVWA LSLVISIGPLFGWRQPAPEDETICQIN EETPGYVLFSAALGSFYLPAILVMYC RVYVVAKRERGLKSGLKTDKSDS EQVTLRIHRKNAPAGGSGMASAKT KTHFSVRLKFSREKKA AKTLGIVV GCFVLCWLPFFLVMPIGSFFPDFKPS ETVFKIVFWLGYLNSCINPIIYPCSSQ EFKKAQFQNVLRQCLRRKQSSKHAL GYTLHPPSQAVEGQHKDM*
495	5992	A	511	928	1311	AMIVPTAVQPGRQSKDPVSKEKKE KARKERWLGTVAHSCNPRTLGGQG GWIMRSRDRDHPGQQGETPSLLKM QKLAGRGGGHQSRLLRQENG NPGGGACSEPRWHCTPAWATE*D



SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						SISNNKK
496	5993	A	512	23	288	APSPDAMGHFAEEDKATITSLWGK VNVEDAGGETLGRLLVVPGLTKL NSSLG*Q*FGGCILSPHHCLGKGRK CFFSIVEMLVILYFM
497	5994	A	513	20	207	LDAGTACAETMACTSRLYGLPRST WPNHPDAILPEGYFSSEI*SRPDCGL RVIYRGLTISSA
498	5995	A	514	228	375	CVALGAMRGMRRLPAGAPKMLMG V**ELDRLGYIAHPQLGKRARAGIV L
499	5996	A	515	417	573	ETPTGLRGGTCL*S*LPRRLRWENC LNPGGRCSEPRSHHCTPAWATEQ DS
500	5997	A	516	173	420	LLLANQLMSLQIRQNYSTDLEAAV NRLGNLDLQAYTYLYLGFYYDRD DEGLEGVSHFFRELAEDKRDY*RL LTMQNQRGG
501	5998	A	517	3	415	HEGHQYAPNPDAMGHFTEEDKATI TSLWIKVNEENAG*ETLARLLAGYP WTQRIFDRFGNLFASDIMGNSPVQ AHGKNVLTSLDATHLDDLKGTGTF AQLSELHCYKLHVDPENFHALANE LATALAMHFR**FTP
502	5999	A	518	3	232	
503	6000	A	519	1	2361	
504	6001	A	520	4806	5788	HTLFGDKLCTVATLRETYGEMADC CAKQEPERNECFLQHKDDNPNLPR LVRPEVDVMCTAFHDNGETFLKK* VIRCL*FKIKKHGVTP*ANTL*KLP* QKYFQH*DLEVLL**FFKEVVFDTT KFYTAKNMIKDILKFJETGYNLSQK FKIDKFFNVFRRYVYVVIIDFVLV SNIILPKFNHLCTHTHTHTLTLFST YLKNDRDKTIMCKLSLIG*LAESEF GGGENVDYNYFCNIVCYRK/ADCF SFLKFRYLYEIARRHPYFYAPELFF AKRYKAAFECCQAADKAACLLPK VLCTRIEKKSLLSNLILSILWDLGT LSV
505	6002	A	521	151	364	VTHDCICYLQQTHF*PKDKNRLKLK RCKKQFHENSQKRVEVALLISAQ RDLRSKIDTEGKSIQQRKKSSC
506	6003	A	522	925	1168	SQHFGPRWVDHLRSGIGDQPGQH GETPALLKIQKLARCGYMRL*SLRR LRRENHLNPGGGGCSETRLHHCIPA WATEQDS
507	6004	A	523	142	329	THSLFLLWSLSHHSPTVNTTLRNLG ALHRRHGKL*AAETLDVFNLTSSES LLFNPFFYRNFR
508	6005	A	524	108	283	KQNLILSPRLKCNBPISVN*NFNLP LTRSQA*ASREAGTTGTCYHA**IG* IFIIDG
509	6006	A	525	1	345	GTRAAPLRIQSDWAQALRKDEGEA WLSCHPPGKPSLYGSLTCHGIVLYG IP*ATSSHRFIANDPNIITSHSSRPTVF VPSSFSSLILFFLAHPLSISLPFFSLPA

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						FPLNFLPLRS
510	6007	A	526	3	276	HEPRRPQYSSGRRAAWLSYSLFSAG CGASAPRPLVMSDSGSYGKSDVEH LYYRNY*STRI*GYIQTSHI*SG*GM TTDSYYGINIFYKLQ
511	6008	A	527	2297	2435	LKLVSKKRVYNFILLLML*TYFLK DGLFECLWHLTCKKKKLQKNP
512	6009	A	528	123	317	QETKKEQNKENKQIK*RSTRKKHR QGTNKTKERGERQTPVGNRQTPT LGIHARPRRRATTSPRA
513	6010	A	529	787	1069	FASHFGRLRQADPLRSGVQDQPGQ QGETPSLLKIQKFPRRDGGRL*SQLP RKLRQENCFNRGGDCSEPRLCPL PAWATERNSVKGERKEKK
514	6011	A	530	110	369	CWLSCCLEVRSCLYTFLSAYNFKCV LTI*HTFFVFFWSLCVYYFFIVLCCL VLVWCLSSLYYGHVYYLYFCYSLFI VLGYGILAV
515	6012	A	531	268	331	QM*TAKCARCEGLGLITLCLDCIVA NTLLVPNGETSWTNTNHLTLQVW LKDGYIGWGLMALCTGIAPVLAGG KDCCGARRCGNR*QMLRYDFS*AL VVLGAIYWLS
516	6013	A	532	807	1060	SWHFGRLRWADYLRPGAGDQLSQ HGEISSLLKTQKLPGCGDTHL*SQLL GRLRQENHLNLGGGGCSEPRSHHC TSAWVTERDSV
517	6014	A	533	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMTGTVASALSSRYH
518	6015	A	534	38	550	APSPDAMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF VDSFGNLSSA\SAIMGNPVKVKAHGK KVLTSLG\DAIK\HLE*SQGAPFAQA *SELH\CDKPALLDPGGTFKLPGENV AGLTVFGQSHFRAKEFHP*RLQAS WHKQKMAEDGDLELASALVPSRY H
519	6016	A	535	2	348	ARAGAGRLRRAASALRLLSPRLPVR ELSSLARLYPHRVDDHYENPTNAGS LD*TSKNVGTGLQLAPA*GDVVKL QTLVDEKVKNVDAFRTLGCGLSAI AYSSLATEWVTGKTADE
520	6017	A	536	385	536	RMSAGALFIGYCIYFDHKRRSDPNF KNRL*DGRKKQKLAKERAGLSKLP D
521	6018	A	537	123	705	AAPTALRVRGPPLLRGPCRHRPRSA FVEKMGVGRNSAIAAGVCGALFIGY\ CIYFDPQKTK*TPTFKNRLRERRK\K QNLQCRRELGL\SKLPD\LKDAESCC RKFFL*RNTSLGEELLSFDG*/YEY*E RAVDHLDKLP\IAV\CGQ\PPQ\LLQV LQQT\PPPVF\QMLLTKLPTISQRIV SAQSLAE\DDVGMRNKLCH

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
522	6019	A	538	1	430	
523	6020	A	539	42	373	
524	6021	A	540	1	430	QQQLQRLVHPDFFSQRSTQTEKDFSEK HSTLVNDAYKTLAPLSRGLYLVS* SS/YGIEIPERTDYEMDRQFLIEIMEI NEKLAEAESEAAMKEIESIVKAKQK EFTDNVSSAFEQDDFEEAKEILTKM RYFSNIEEKIKLKKIPL
525	6022	A	541	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSFGNLSSA SAIMGPNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVLAHFGKEFTP EVQASWQKMVTGVASALSSRYH
526	6023	A	542	38	547	APSPDAMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQR FFDFSFGNLSSASAIMGNPKVKAHGK KVLTSLGD\AIKHL\DDLKGTFAQA *SELH\CDKAALLDPENFKLPGGNV AG*PVFGQSHFRAKEFHPWRLQGF GISRRWQKMVTWSWPVPCSSRYH
527	6024	A	543	328	495	NLGANNCSLLGIGLLKGSMGRLW PKAFSAG*KQGLQNQRKHTALVKIE DVDA*GE
528	6025	A	544	154	340	PGLLKAAIWGIAYLRTYWTYVLA DLHPFADMLHAGYSITSEVEQPVLA VQLTYNPDES*WP
529	6026	A	545	124	323	EVKSVYLVYILSNRFF*CTYMHILV YYVYFIGLTI*LEEHSMLVYQNLVH YFLVFNVGIIYLLYLV
530	6027	A	546	314	445	SPILLQFTVVLTTRYLFTKIQFIYFFET ESCSIAQARV*WCDLG
531	6028	B	547	1	1011	MDLKFNNSRKYISITVPSKTQTMSP HIKSVDDVVVLGMNLSKFNKLTQF FICVAGVFVYLIYGYLQELIFSVEG FKSCGWYLTLVQFAFYSIFGLIELQL IQDKRRRIPGKTYMIIAFLTVGTMG LSNTSLGYLNYPTQVIFKCKKLIPV MLGGVFIQGKRYNVADVSAACMS LGLIWFTLADSTTAPNFNLRVLYSY SIGFVYILLGLTCTSGLGPVTFCAK NPVRTYGYAFLFSLTGYFGISFVLA LIKIFGALIAVTVTTRKAMTIVLSFI FFAKPFTFQYVWSGLLVVLGIFLNV YSKNMDKIRLPSLYDLINKSVEARK SRTLAQTV*
532	6029	A	548	244	1408	SRHNGMDLTQQAQDIQNITVQETN KNNSIESCKITMDLKFNNSRKYIS ITVPSKTQTMSPHIKSV*RVVVLGM NLSKFNKLTQFFICVAGVFVYLIY GYLQELIFSVEGFKSCG\WYLTLVQ FAFYSIFGLIELQLIQDKRRRIPGKTY MIIAFLTVG\TMGLSNTSLGYLNYPT QVIFKCKKLIPVMLGGVFIQGKRYN VADVSAACMSLGLIWFTLADSTTA PNFNLTGVVLISLALCADA VIGNVQ EKAMKLHNASNSEMVLYSYSIGFV

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						YILLGLTCTSGLGPAVTFCAKNPVR TYGYAFLFSLTGYFGISFVLALIKIF GALIAVTVTGRKAMTIVLSFIFFAK PFTFQYVWSGLLVVLGIFLMFTAKI WDKIRLPSLV
533	6030	A	549	66	346	IQQLPTFFHIFSIFLLIR*FFYMKGFR* LVLFYICPHVYA*SYFSLFFCSLTI* FISFSLYFTLFLFFFTLLFICVLAMFI FFELHLSYIP
534	6031	A	550	21	337	GPEAQCPDQPPPWLSFQGLPQGGT WATHSAPCSPNLTSSWCSDSEPGR AGGRGRPPTLDHDAPPTTPL*PSKP HPCIPQALPSSRTLRLPLATPRQHAA TQCTP
535	6032	A	551	526	771	PPPLGVPGTLQFLRPRAAVLIGSKLL RPGRFCRWIFSPLLLVNISWLGTVV HACNPSTLGDQGGGRIT*G*EFETSLP TWRNS
536	6033	A	552	305	569	KKPLKGEKGGSLKTRPSFKKPDARI YLKKSVMGFL*TNPEQFKKEIRNTIPLI KGASSSSSSKTNLGINLTKVVKDLN NENSRTLLRQS
537	6034	A	553	90	339	EVSALPDLPAVMLAGPTP*PSFPRTP SYFSAPPLLLPLSCSFPLPLPMPHSC PPSSSPSPSLLLSITPSPAPSPFPLLF P
538	6035	A	554	1179	1408	GYPVGKRRRLGERQGPQPPTLLPCD KEAERGEHIYIYFIYILYI*YIYNIYII YIYNIYIHIYIYIYIHTYIYI
539	6036	A	555	722	991	SQHFWRPRQVNVHSLGVQDQHGQ HSENPVSTKIYIYIQLARCSDRCL* S*LLRRLRHENHLNLGGGGCSELKS CHCTPAWATE*DPVSK
540	6037	A	556	1	362	GTSRQVCREHSFQSVKLSAGARSW CFLSHWDPAGEVSLTDCSEIFLPFLG MAAVYHYFSINIFFKTSFFRLILYI** SYFHLFLYYSILCLFILLFIIFYC YILFISNLFTHFLFL
541	6038	A	557	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
542	6039	A	558	38	497	APSPDAMGHFTEEDKATITSLWGK\ VNVEDAGGETLGRLLVVYPWTQRF FDSFGNLSASAIMGNPKVKAHGK KVLTSGLDAIK\HLDDLKGTFAQA *SELALVDKLACGILENFKAPGEML LVTRFWQSHFRQKNFTPEGCKASW AERWVTW
543	6040	A	559	1	414	FETVSLLLLRLEHTGTISTHCNLRP GSNDSAASAS*VAGTTSVCHHTGLI SVFSIETEFHHVVGQTGLELLTSSDPL TSASPGAGIKGGSHCAQSPICFRGN NEMNYQATGIYSKSEIFFCLGYVTM SRCLTSQSGS

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
544	6041	A	560	178	334	NVCRLPVTNAESDAMINDAIRPINF TGFLTMFA*NLTGADPADVIIA AFDVL
545	6042	A	561	322	649	
546	6043	A	562	3	452	
547	6044	A	563	24	587	GIPQTQREPTMVLSPADKTNV KAAWGKVGAHAGEYGAELER MFLSFPTTKTYFP HFDLSHGSAQVKGHGK KVADALTNAVAHVDDMPNALSAL SDLHAHKLRVDPVNFKLLSHCLLV TLGA\HLP AEFTPAVHA\SL\DKFLAS VSTGLATSKYPLSWSPR WPCFLAPWASPQPLLP FPAPVPPWSLK
548	6045	A	564	3	474	
549	6046	A	565	1099	1243	
550	6047	A	566	425	943	MGRSAPVEISYETMR FMMTRNPTNATLNK FTEELKKYGVTT LVRVCDATYDKAP VEKEGIHVLDW PFDDGAPPPNQIV DDWLNLLKTK\F REGARVCVA\VH CVGRVGE GAPVL/VLALAL DWNVGMK\YED A\QFIRQKRRGA FNSKQL\LYLE EYRPKMRLRFR DTNGHC\CVQ
551	6048	A	567	1	441	
552	6049	A	568	1	890	MSKSESPKEPEQLR KLFIGGLSFET TDESLRSHFEQW GTLTDCVVMRDPN TKRSRGFGFV TYATVEEVDAAMNA RPHKVDGRV VEPKRAVSREDSQ RPDYFEQY GKIEVIEIMTDRG SGKKRGFAFV TFDDHDSVDKTVI QKYHTVNGHN CEVRKALSKQEMAS ASSSQRG RSGSGNFGGGRG GGFGGNDNFGRG GNFSGRGGFGG SHGGGGYGGSGDG YNGFGNDGSNFG GGGGSYNDFGNY NNQSSNFGPMKGG NFGGRSSGPYG GGGQYFAKPRNQ/ GGYGGSSSSSY GSGRRF
553	6050	A	569	579	2102	SPKEPEQLRKLFIG GLSFETTDESLR SHFEQWGT LTDVCVVRFG RDKA VKQPISLAYLGA VFSECL*K*LIAL* LELCWQRNVLL* F*KLTS*I*G* WETGRTFYKRLV* SFLLPYSKLK* QKLLRSDFV LHKLTLFSG\MR DPNTRKSRGFGF VTYATVEEVDA AMNARPHKVDGR VVEPKRAVSRE VSGFFFFFLNLLG YVLL*T*DSGVF* TYQNFLFEYRLC* SKPMVFLLLADS QRPGAHLT/V* KKIFVGGIKRRHL KEHHLRDYF\EQY GKIEVIEIHDLTR GSGKK\RGFAFV TFDDHDSVDKIV SKYQIVAFSKGST ICMAF*TLIPCCI YVFFLVQKYHTV NGHNCEVRKALSK QEMASASSSQRG MLVA*LNLKGNFEL LQYE*FNA*TSCL KV/ESGSGNFGG GRGGFGGNDNF GRGGNFSGR/GYV WFIYM*F*LLTIF AMKILQYGNCIQ NVTLSPSHT*NLK LFLTGGFGGSRG GGGGYGGSGDGYN

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						GFGNDGKFFRNK
554	6051	A	570	250	381	
555	6052	A	571	249	468	PNQRLKWKS*LMGQGRG*KWKLL VLFYHKA*RMWPA\C\CLDLGLGTG \CTC\CLLVYANWLHLLFLCLCPYP WLS
556	6053	A	572	2	488	QEPAHDLRMYGKIIFVLLLSEIVSIS ALSTTEVAMHTSTLLPSSHKRVTSS S\QTNGETGTTCPIVSLYPAPCSNT HYFVCDGWYYWNPDLNFLLYSMT DKGMRMWPACCLILPR\TSCCTCSL AYANWLHL\FL\CLCPYPWAILNS LFSWPSLITGILYF
557	6054	A	573	7	412	
558	6055	A	574	3	479	NWELLWLLVLCALLLLLVQLLRF LRADGDLTLLWAEWQGRPE/WEL TDMVVWVTGASSGIGEELAYQLSK LGVSLVLSARRVHELERVKRRCLE NGNLKEKDILVPLDLTDTGSHEAA TKAVLQEFGRGFFNGLRTELATYPG IIVSNICPGPVQSN
559	6056	A	575	1	321	
560	6057	A	576	2	1243	GAASAEPGAPEPLLPACSLGGAGA VRLWAGRRGGAAIPQGSATLVRA VFFPPSWACAAAMNWELLWLL\V LCDVLLLLVQLL\RFLRADGDLTL LWAEWQG/RDRPEWELTDMVVW V\TGASSG/ILGEELAYQLSKLG\VSL VLSAR\RVHELEKGEKERCL\ENGQF LKEKDITLFLPL\DLDP TLGSH*SRLT KAVLQEVLRIDILGSTMVGM\SQR SL\CMDTSLDVYRKL\ELNYLGTVS LTKC\VLPHMIERKQGKIIVTNSILG IISVPLSIGYCASKHALRGFFNGLRT ELATYPGIIVSNICPGPVQSNIVENSL AGEVTKTIGNNGDQSHKMTTSCV RLMLISMANDLKEVWISEQPFLVT YLWQYMPTWAWWITNKMGGKKRIE NFKSGVDADSSYFKIFKTKHD
561	6058	A	577	175	354	
562	6059	A	578	2018	2182	
563	6060	A	579	140	287	MVKRNQCPSLPPN*KMRSQGSTCQ PHCQRWLPSTRSYTHPLKARPSA S
564	6061	A	580	357	760	
565	6062	A	581	182	459	
566	6063	A	582	1	382	
567	6064	A	583	3	406	
568	6065	A	584	173	415	
569	6066	A	585	2	424	
570	6067	B	586	108	395	VGAHAGEYGAELERMFLSFPTTR TYFPHFDLSHGFCPLRGHGQEGGR RADQRRGARGTTCPTLSALS DLHA HKLSSGTRFNFQAPKATGLLG*
571	6068	A	587	379	579	
572	6069	A	588	2	366	SLPASDRPPISSPLATSGTIFSAISCF WDLPAFLWLAPSCQPTMSSQIRQN

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						YSTDVEAAVNSLVNLYLQASYTYL SLQDIKKPAEDEWGTKPDAMKAA MALEKKLNQALLDLHALGSART
573	6070	B	589	220	480	MSSQIRQNYSTDVEAAVNSLVNLY LQASYTYLSLGFYFDRDDVALEGV SHFFRELAEKREGYERLLKMQNNQ AWRPRSLPGHQEAS*
574	6071	A	590	142	383	
575	6072	A	591	1	308	
576	6073	B	592	195	326	MMGVLDGVLMELQDCALXLLKDV IATDKEDVAFKDLDVAILVV*
577	6074	A	593	5	1199	PDSRLRLHLFLKSPQFSIMSEPIRVL VTGAAGQIAYSLLYSINGNSVFGKD QPIILVLLDITPMMGVLDGVLMELV RLCPSPPERCGNGSVFGKDQPIILVL LDITPMMGVLDGVLMELQDCALPL LKDVIAITDKEDVAFKDLDVAILVGS MPRREGMERKDLLEY/ADVKIFKSQ GAALDKYA\QKSGKVIVGGNPANT DCLTASKPAPCIPKENFSCLTRLDH NRAKAESGLRLVVTADHDGQNGIIW GNHSSTQYPDVNHAKVKLQGKEV GVYEALKDDSWLKGEFVTTVQQR GAAVIKARKLSSAMSAAKAICDHV RDIWFGTPEGFEVSMGVISDGNISY VPDDLVSFPVVIKNTWKVFVEGLP INDFSREKMDLTAKELTEEKESAFE FLSSA
578	6075	A	594	46	298	
579	6076	A	595	982	1193	
580	6077	A	596	69	399	VSNYPTVGCCIFLQIRARNPAFQPQT LMDFGSGTGSVTW*VTFFSPILVNF SSRKPYLHHSKINRLNQRENQVVG NL*CFHFQIRQGRRRYMDWGQNLK EMSSKKRRMY
581	6078	A	597	600	887	
582	6079	A	598	813	973	
583	6080	A	599	166	437	ADHLKSGV*DQPGQHGEILSLLKLQ *FPGRGGAHL*SLLGRLKQENHLN PGGGGCSEPRLCWTPVRATVGD VQKK*KSQDGPRAKLG
584	6081	A	600	3	238	SGDRDHPG*HSETLSLLKIQQNIAGR GGGRL*SRLRLRLRQENGVSPPGGG ACSEPRSHHCTPAWETERDSVSKK KKKKL
585	6082	A	601	4005	4345	SQHFGRRPRADHLRSGVQDQPDQH GETPSLLGGRGGGRITKSGDRDHPG* HGETPSLLKMQ/EKLAGRGGGRLW SLLGRLRQENGVSPPGGRACSEPRS CHCTPAWLTEQDSVSKK
586	6083	B	602	1	9234	MGAPTLPPAWQPFLKDHRISTFKN WPFLEGCACTERMAEAGFIHCPT NEPDLAQCFFCFKELEGWEPDDPI EEHKKHSSGCAFLSVKKQFEELTLG EFLKLDREKAKNKIAKETNNKKKEF EETAKKVRRAIEQLAAMD*
587	6084	A	603	1577	2233	SGCLLSPPSVGRQNSPVELGGAGLS

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						RAGWAPQERGRAALLLISPGPNVR GGPDWLPSVLQMRGLPLWDLGGRP DVGRMSPGGRPGSCWATQLRFHIS LAPLFSWAGRSGSRLNPSTLGGRGG PITRSGDRDHPG*HGETLSLLKIQKI SQACWR/CACSPSYGRLRQENGVPN GGGACREQRSGHCTPAWATEQDSV SKKKKKKSGSTIRLKHILHKII
588	6085	A	604	151	454	FQKIGPGAVAHACNPSTLGGRSRRI TRSGGRDHPG*HSETPSLLKIQ\KLA GRGGGCL*SLLWRLRQENGVPNPG GGACSEPRSRHCTPAWVTERDSVS KKK
589	6086	A	605	1362	1647	
590	6087	A	606	10289	10708	SQHFGKLRQEDHLRSGVREQPGQH GKTPYLLKIQKLARRSGACL*SLL RRLRQENRLNPGGVGCSEPRLLHC TTAWTLQ*DPVSKKLKKYIERQR YHQHMKHPWSTKIQYVCMG*HR SVEKQIIQTLCMFVFTHTY
591	6088	A	607	709	980	
592	6089	A	609	234	381	PPWTQFSLSCVCLL/CSRPA/VSAWR QARENESQAKGETAYETITSCENRS H
593	6090	A	610	1	1755	
594	6091	A	611	1128	1321	
595	6092	A	612	650	800	
596	6093	A	613	149	475	
597	6094	A	614	1	801	
598	6095	A	615	1284	1386	
599	6096	A	616	20	3888	
600	6097	A	617	204	411	
601	6098	A	618	1	1468	
602	6099	A	619	48	178	
603	6100	A	620	79	1953	LQVGTASSLLLSRVFGDRGYSPET RKCPKPINVRVTMDAELEFAIQPN TTGKQLFDQVVKTI RPSRQVWYF\G LHYVD\NKGFTWLKLDKKVSAQ EVRKKNPLQFKFR/APKFYPEDVA\ EELIPGTFTQKLFF\QVEGRESLSDE DLLAPLETGRALWGSYACASPRLG DYNK/EKLHKSGVPSASERLIPQRV MDQHKLTRDQWEDRIQVWHAHR GMLKDNAMLEYLKIAQDLEMYGIN YFEIKNKKGTDLWLGVDALGLNIY EKDDKLTPKIGFPWSEIRNISFNDDK FVIKPIDKKAPDFVFYAPRLRINKRI LQLCMGNHELYMRRRKPDITIEVQQ MKAQAREEKHQKQLERQQLETEK KRRETVEREKEQMMREKEELMLRL QDYEEKTKKAERELSEQIQRALQLE EERKRAQEEAERLEADRMAALRAK EELERQAVDQIKSQEQLAAELA EYT AKIALLEEARRRKEDEVEEWQHRA KEAQDDL VKTKEELHLVMTAPPPP PPPVYEPVSYHVQESLQDEGA EPTG YSAELSSEGIRDDRNEEKRITEAEKN



SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						ERVQRQLVTLSSSELSQARDENKRTH NDIIHNENMRQGRDKYKTLRQIRQ GNTKQRIDEFEAL
604	6101	A	621	269	361	
605	6102	A	622	210	367	ISQSGDCCSVWLSLQGPCKGCPKP/I PSPGLQPRATPPA*VQRTSHPMSC SN
606	6103	A	623	1792	1935	
607	6104	A	624	9	326	
608	6105	A	625	250	381	
609	6106	A	626	155	457	NQKELGNTPRYPLEASNWLQPVKD WPVTNQRLKWKS*LMGQGRG*KW KLLVLFYHKA*RMWPA\CCLDLGL GTG\CTC\CLLVYANWLHLLFLCLC PYPWLS
610	6107	A	627	2	488	QEPAHDLRMYGKIIFVLLLSEIVSIS ALSTTEVAMHTSTLLPSSHKRVTSS S\QTNGETGTTCPIVSLYPAPCSNT HYFVCDGWYWNPLNLLYSMT DKGMRMWPAACCLILPR\TSC\CCSL AYANWLHL\FL\CLCPYPWAILNS LFSWPSLITGILYF
611	6108	A	628	2	364	
612	6109	A	629	946	1142	LSGIIHYSFFTIRNIKALFSLC*VFQF GFLRDFPFIFPFIFRKPILTKGPTSVA M*WKGGIHFIA
613	6110	A	630	946	1193	LSGIIHYSFFTIRNIKALFSLC*VFQF GFLRDFPFIFPFIFRKPILTKGPTSVA M*WKGGIHFIA*SAFPVQGLLFRS WNL
614	6111	A	631	946	1142	LSGIIHYSFFTIRNIKALFSLC*VFQF GFLRDFPFIFPFIFRKPILTKGPTSVA M*WKGGIHFIA
615	6112	C	632	294	710	MVRSRQMCNTNMSVPTDGAVTTS QIPASEQETLVRQESDYSQPSTSSSI IYSSQEDVKEFEREETQDKEESVESS LPLNAIEPCVICQGRPKNGCIVHGKT GHLMACFTCAKKLKRKNPCPVCR QPIQMIVLTYFP*
616	6113	C	633	822	1149	MLVLHICLLLTIIRGFRAWSRGLKT PQFPSRGLTTAEARRPGPRGSFHSFG QGTGRSYALIRGGTVLLAAKAAGS RSEGSRPPLGLGFLHLSDTQGHGTG PRSSQARAV*
617	6114	A	634	5	76	
618	6115	A	635	269	354	
619	6116	A	636	184	299	FFCTFSTDGVSPC*PGWSRSPDLVIH SPRPPKVLGLQA
620	6117	A	637	3	307	ESCSEAQAGVQGAQSWLTATSSSQ VHAILLPQPPK*LGLQVPATTPG*FF VFLVETGFHCVSQDGLKLQTS*SAH LGLPKCWDYRHEPLRPAKKQLFKN VP
621	6118	A	638	2	131	SKAALTGSGPGP/IPLCFVSAVLAPFI RPS*SLLAGRLDGGQD
622	6119	A	639	1	822	
623	6120	A	640	1258	1454	LSGIIHYSFFTIRNIKALFSLC*VFQF

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						GFLRDFPFIFPFIFRKPILTKGPTSVA M*WKGGIHFIA
624	6121	A	641	248	386	SARLSLPKIWDYRREPLHPARSFFIY SSSSILY*S*LVSITALLF
625	6122	A	642	132	243	LGLQVPATAPG*IFFVFLVETGFHH VSQDGLDLLTS
626	6123	A	643	397	954	
627	6124	A	644	1	1388	
628	6125	A	645	2285	2409	
629	6126	A	646	36	224	
630	6127	A	647	242	933	YGESKDOWNQKDLLSALVLTTVNCL PTPIMAKSAEVKLAIFGRAGVGKSA LVVRFLTKRFIWEYDPTLESTYRHQ GNHSMMEVVSMGGY*DTAGQEDTI QREGHMRWGEFVLVYDIT*PRKF LKEVLALKEHLDEIKKPKNVTLILV GNKADLDHSRQVSTEEGEKLATEL ACAFYECSACTGEGNITEIFYELCRE VRRRRMVQGKTRRRSSTTHVKQTI NEMLTKEISS
631	6128	A	648	596	709	
632	6129	A	650	1	367	
633	6130	A	651	135	307	
634	6131	A	652	170	372	
635	6132	A	653	3	320	
636	6133	A	654	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSFGNLSSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
637	6134	A	655	52	518	APSPDAMG\HFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF DFSFGNLSSASAIMGNPKVKAHGK KVLTSLGDAI\HLLDDLKGTFQAQLSE LHCDKLHVDPENLKLGNVLETAL AIQFRRKNSPL*GQASWQKMVTGV ASALSSRYH
638	6135	A	656	123	219	
639	6136	A	661	413	545	
640	6137	A	662	4	350	
641	6138	A	663	1034	1091	
642	6139	A	664	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSFGNLSSA SAIMGNPVKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
643	6140	A	665	38	602	APSPDA\MGHFTEEDKATIT\SLWGK VNVE\ DAGGETLGRLLVVYPWTQR FFDFSFGNLSSASAI\MGNPKVKAHG KKVLT\SLGDAIK\HLLDDLKG\TFAQ A*SELHL*QSCNVDP\ENFKAPGEM LLVTR/VLAIPFSAKEFTPEGCRASW AERWVTCSWPVALFLQDITTEAQLP MNAELFKDKAFILASNYK
644	6141	A	666	24	452	APSPDAMG/HSLWGKVNVEDAGGE

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						TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
645	6142	A	667	38	536	APSPDAMGHFTEEDKATITSLWCK VNVE\ DAGGETLGRLLVVYPWTQR FFDSFGNLSSASAIMGNPKVKAHG KKVLT\SLGDAIKHL\DDLKG\TFAQ A*SEL\HC*QAGMWD\ENFK\LLGE MLLVTRFGQSHFRQKNFTPEVARL SWAERWVTWSWPSALVPSRYH
646	6143	A	668	132	357	
647	6144	A	669	1	89	
648	6145	A	670	136	594	LNRVAFLPGA AVILIGHLHTHTGPS GVCNVSMRGFSSPAGWTP TGS HRG KERPAGRLMHRRMGWSAVEWTG\ AQGIPCISTC PERTGGDAATRSRPP VLPPPPRPPQRRCRHLVSRA GTPRC ACAGTLTSKRGTHWRSTELLRRSP LRSSQ
649	6146	A	671	400	696	
650	6147	A	672	120	352	
651	6148	A	673	276	401	
652	6149	A	674	139	470	
653	6150	A	675	136	1058	GVVGAAASGAGSRKAGLAGVPGPP GRANRESPPGPVAMGRVIRGQRKG AG\SVFRAHV KHRKGAARLRA VDF AERHGYIKG\IVKDIIHDPGRGAPLA KV\VFRDSYRFKKRTELAFIAAEGVH TGQF\VYCGKKAQLNIGNVLPVGT\ MPEGTIVC/CALEEKP\GDRGK\LAR ASGNY\ATVISHNP\ETKKT\RVKLPF RVQRR LSPSANKSLWLVLVAGGWP ECDKPILKAG\RAVPQI*RQKRNCW \PRVTGVWAMNPF EAFFLKGGNPPA HRQSPPIRRDAPAGRKVGLIAARR TGRLRGTKTVQEKEN
654	6151	A	676	21	340	
655	6152	A	677	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
656	6153	A	678	38	529	APSPDAMGHFTEEDKATITSLWKG VNVEDAGGETLGRLLVVYPWTQR FDSFGNLSSASAIMGNPKVKAHGK KVLTSLGDAIK\HL\DDLKGTFQAQ DVNLHC*QACMLDPENFQASWGN VL\VTRFWAIPFSGKEFHP*RCQAFL GRKMGDLELASALVPSRYH
657	6154	A	679	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFQAQLSELHCDKLHVD PENFKLLGNVLVTVLAIHFGKEFTP

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						EVQASWQKMVTGVASALSSRYH
658	6155	A	680	3	545	HSLFGTSEVINKLRSPDA\MGHFTEE DKATITSLWGKVNVE\ DAGGETLGR LLVVYPWTQ\ RFFDSFGNLSASAIH GQPPKSRHMGKKVLTSLGDAIKHL \DDLKGHLLPKPEVKLH\CDKAALL DPEELSSFLGEMLLGDPFLGNPIFGQ KNFTP\ EVARLSWAERWWTWSWPS ALVPSRYH
659	6156	A	681	1	432	
660	6157	A	682	334	845	AVRVRYVAFRYRAPRAVCLRLWSC RREVIHVPVRGKQGGKVRAKAK\ S RSSPRGPCRFPVGPSCTELLRK\ GNY AER\MSGAGAPV*LGGRCLKYLTAE IPEAWLANAAA*QRRPRIIPRHLS SPIRNDEGS*TKLLGQKLTV\AQGGV LPNIQ\AVLLPKKDGESEGRRSK
661	6158	C	683	392	445	MQPAVQVRVGNLSRYFPS*
662	6159	A	684	183	481	
663	6160	A	685	253	385	
664	6161	A	686	256	374	
665	6162	C	687	354	416	MKESPGGELPQTGKKPVFLF*
666	6163	A	688	2	171	
667	6164	A	689	320	584	TRLPFDRPRATGCHQVPVSERRSPIS QDRLTHVQLLFTWNPSP\LRPSKFSF EYLL\PPRSCTCGGSHPGPKP*ASR LTAAALLLVAA
668	6165	A	690	33	494	
669	6166	A	691	1	522	PLKRSDGCNDGRPTRPPTRPDITTVF TSNLKQTRMVHL\TPEEKSAVTALW GKVNVD\VGKALGRLL\VVYPW\ TQRF\FE\SFGDLSTP\DA\VMGNPKV KAHS\KKVLRGAF\SDGLAHL\DNLK GTF\AHT\EVSLHCDK\LH\VDP*RTFR LLGQRAW SVVAGPIHFWQKNFNPT SCRLA
670	6167	A	693	241	1104	
671	6168	A	694	95	462	
672	6169	A	695	33	494	
673	6170	A	696	1	523	PLKRSDGCNDGRPTRPPTRPDITTVF TSIAHTDTMVHLTPVE\KSAVTALW GKVNVD\VGKALGRLL\VVYPW\ TQRF\FE\SFGDLSTP\DA\VMGNPKV KAHS\KKVLRGAF\SDGLAHL\DNLK GTF\AHT\EVSLHCDK\LHRGSLKNFR LLGQRAW SVVAGPIHFWQKNFNPT SCRLA
674	6171	A	697	318	515	
675	6172	A	699	2	648	
676	6173	A	700	137	507	
677	6174	A	701	118	375	VAVVQIIFLPVFIAEKYKDLVPDnsk TADNATKNAEPLINLDVNNPDFKA GVMALANLLQIQRHDDYL\VMLK\A IRILVQERLTQD
678	6175	A	702	1	969	AATVLT TIGEAPSRSDSAPARPLAA SPVPAPPAPPRFFSPGRGPVDQSEKR WTFMRRLT\SLDYHNPAFNCCKD

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						ETEFRNFIVWLEDQKIRHYKIEDRG\NLRNIHSSDWPKEFEKYFKRC*TCPFKIQDRQESYLTGFFGLAVRLEYGDNAEKYKDLVPDNSKTA*QLQLKIAEPLIN\LDVNNP\DFKAGVVGFG*TWLQIQRH\DGLPQMLKANSQFWVQERLDHQGCQFA*GQIKQKRGLPV\A\LDKHILGFDTGDAVLNEAAQILRLHIEELRELQTKINEAIVAVQAIIADPKTDHRLGKSLEDEHLRTSASHLL
679	6176	A	703	105	1591	
680	6177	A	704	110	431	
681	6178	A	705	171	1577	GGNRATIQAGQCGNQIGAKFWGR*SVNEHGIRPHRHPHGDSDPAAWTRNPPVYYNESHKVGK\YVPR\AILGGI*EPGEPWDSVR\SGSFLGPPKGEKIFPPFRPDNFVFGQSGAGNN\WAKRPLAQEGAEL\VDS\VLVDVGTEGRQSCD\CLQGFP*PTSLGRGGTGSGMGTLLEYQGGFEKEYPD\RIMN\TFSVVP\SPKCLDTVVQPYKATLSVHQLVENTDETYCIDNEALYD\ICFRTLKLTTPTYGDLNHLVSATMSGVTTCLRFPGLNADLRKLAVNMVFPRLHFFMPGFAPLTSRGSQQYRALTVPELTQQVFDKNNMMAACDPRHGRYLTVAAVFRGRMSMKEVDEQMLNVQKNSSYFVEWIPNNVKTA\CDIPPRGLKMAVTFIGNSTAIQELFKRISEQFTAMFRRKAFLHWYTGEQMDMEFTEAESNMNDLVSEYQQYQDATAEEEEDFGEEAEAEA
682	6179	A	706	1	558	
683	6180	A	707	1306	1459	LASMCMCWIESHFCPPGPTGGSRRGPP\HLWLPGRSSGRSQRR\LAESTEAPR
684	6181	A	708	1073	1324	
685	6182	A	709	1	797	
686	6183	A	710	1	3210	MVKGSIQQEELTILNIYAPNTGALRFIKQVLRDLQRDLDSHTIIMGDFHTPLSTLDRSTRQKVNKDIQELNSALHQEDLIDIYRTLHPKSTEYTFFSAPHHTYSKIDHIVGSKALLSKCKRTEIITNCLSDHSAIKLELRIKNLTQNRSTTWKLNNLLNDYVWHNEMKAEIKMFFE TNENKDTTYQNLWDTFKAVCRGKFIALNAHKRKQERSKIDTLTSQ\KEL EKQEQTHSKASRRQEITKIRAELEKEIETQKTLQNINESRSWFFERINKIDRPLARLIKKKREKNQIDA\IKNDKGDITDTPTEIQT\TIREYYKHLYANKLENLEEMDKFLNTYTLPTLNQEEVESLNR PITGAEIVAI\NSLPTKKSPGPDGFTA EFYQRYKEELVPFLLKPFQSIEKEGILPNSFYEASIIIPKPGRD\TTKKNFRPISLMNIDAKILNKILAKRIQQHIKNLIHHDQVG\FIPGMQGWFNIRKSINVIQHINRAKDKNHMIISIDA\AEKAFDKI

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						QQPFMLKTLNKLDDMIVYLENPIVS AQNLLKLISNFSKVSQYKINIQKSQA FLYTNNRQTESQIMSELPFTIASKRI KYLGIQLTRDVKDLFK\ENHKPLLN EIKEDTNKWKNIPCSWVGRINIVKM AILPKVIYR/FNAIPIKLPMTFFTELE KTTLKFIWNQKRARIAKSILSQKNK AGGITLPDFKLYYKATVTKTAWYW YQNRDIDQWNRTEPSERTPHIYNYL IFDKREKNKQWGKDSL FNKWCWE NWLAICRKLKLDPFLTPYTKINSRW IKDLNVRPKTIKTLEENLGFTIQDIG MGKDFISKTPKAMATKAKIDKWDL IKLKSFCTAKETTIRVNRQPTKWEKI FATYSSDKGLISRIYNELKQIYKKKT NNPIKKWAKDMNRHFSKEDIYAAK KHMKKCSPSLAIREMQIKTTMRYH LTPVRMAIHKSGNNRCWRGCGEIG TLLHCWWDCCLVQPLWKA VWRFL RDLELEIPFDPAIPLLGIYPKDYKSC CYKDTCTRRKQLDCAEPVEPRKVG DGEWSLTKWTRPGSRALPWPEQA KPYPPTLPTLAQDF
687	6184	A	711	1	2666	MVKGSIQQEELTILNIYAPNTGAPRF IKQVLSLDLQRDLDSHTLIMEDFNTF LSTLDRSTRQKVNKNTQELNSALH QADLIDIYRTLHPKSTEYTFFSAPHH TYSKIDHIVGSKALLSKCKRTEITN YLSDHSAIKLELRIKNLTQSRSTTW KLNLLNDYVWHNEMKAEIKMF FETNENKDTTYQNLWDAFKAVCRG KFIALNAYKRKQERSKIDTLTSQK ELEKQEQTHSKASRRQEITKIRAE KEIETQKTLQKINESRSWFFERINKI DRPLARLIKKKREKNQIDTIKNDKG DITTDPTIEQTTIRESYKHL YANKLE NLEEMDTFLDTYTL PRLNQEEVESL NRPITGSEIVAIINSLPTKKSPGPDGF TAEFY/PESYL*QTHRQYHTEWAKT ASIPFENWHKTGMPSLTPIQHSVG SSGQGNQPGEGNKGY SIRKRGSSQIV PVCRRHDCLSRKPHRLSPKSP*ADK QLQQLRIQNQCTKITSILIHQQQTN REPNE*TPIHNCFKENKIPRNPTYK GCEGPLQGELQTTAQGNKRGHKQ MEEHSMMLMGRKNQYRENGHTAQG NLQIQCHPHQATNDFLHRIGKNYFK VHMEPKKSPHRQVNP KPKEQSWRH HTT*LQTILOGYSNQNSMVLVPKQR YRSMEQNRA LRNNAAYLQLSDL*Q T*EKQAMGKGFPI**MVLGKLASH M*KAETGSLPYTLYKNQFKMD*RF KR*T*NHKNPRRKPRHYH*GHRRG QGLHVQNTKSNGNKSQN*QMGSN* TKELLHSKRNYHQSEQATYNMGEN FRNLLI*QRANIQLQ*TQTNLQEK NKQPHQKVGEQHEQTLLKRRHLCS QKTHEEMLITGHQRNANQNHYEIS

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						SHTS*NGNH*KVRKQQRQNS
688	6185	A	712	1	4371	
689	6186	A	713	1	1849	MVKGSIQQEELTILNIYAPNTGAPRF IKQVLSDLQRDLDSHTFIMGDFNTP LSTLDRSRRQEVNKDTQELNSALH QADLDIYRTLHPKSTEYTFFSATHH TYSKIDHIVGSKAVLSKCKRTEITN YLSHSAIKLELRIKLTQNRSTTW KLNNLLLNDYWVHNEMKAEINMF FETNENKDDTTYQNLWDTFKA/EIQA TIREYYK\HLYTNKLENLEEMDKFL DTYTLPRLNQEKVESLNRPTGSEIV AIINSLPTKKSPGPDGFTAIFYQRYK EELVPFLLKLFQSIEKEGILPNSFYEA SIILIPKPGRDTTKKNFRPISLMNID AKILNKILANRIQQHIKKLIHHDQVG FIPGMQGWFNICKSINVIOHINRTKD KNHMIISIDAEKAFDKIQQPFRLKTL NKLGVVDGYLKIIRAIYDKPTANIIL NGQKLEAFPLKTGTROGCPLSPLLF NIVLEVLAIRAIRQEKEARDVKDLFK ENYKPLLKEIKEDTNKWKNIPCSW VGRINIMKMVILPKDSTWAEVLVG DRRSGRLTEMLVIFLVFQSFHSFLN TLMSLPSIFSSWPCFCSSQLVSLRT CRSVCLSSAAGVSRVASLGNQKKR DLGSENL
690	6187	A	714	1	1825	MVKGSIQQEELTILNTYAAHTGAPR LIKQVLSDLQRDLDSHTIIMGDFNTP LSTLDRSTRQKVNKDTQELKSALH QADLTDIYRTLHHKSTEYTFFSAPH HIYSKIDHILGSKALLSKCKRTEITN YLSHSAIKLELWIKNLTQNHSTTW ELNNLLLNDYWVHNEMKAEIKMFF ETNENKDDTYHNLWDTFKA VCRG KFIPLNAHKRKQERSKIDTLTSQKE LEKQEQTHSKASRRQEITKIRAEK EIETQKTLQKINESRSWFFERINKID RLARLIKKKREKNQIDAINDKGD ITTDPTIEIQTIREYCKHLYANKLEN LEEMDKFLDTYTLPRLNQEEVESLN RPITGAEIVAIINSLPTKKSPGPDGFT AKFYQRYKEELVPFLLKLFQSIEKE GILPNSFYEASIIIPKPGRDTTKKN FRPISLMNIDAKILNKKLAKRIQQHI KKLIHHDQVGFIIPGMQGWFNIRKSI NVIQHINRAKDKNHMIISIDAEKAF DKIQQPFMLKTLNKLGIKYLGIHLT RDVKDLFKENYKPLLKEIKEDTNK WKNIPCSWVGRINIVKMAILPKNILI TLQLLLVLPELSTLIPLWLPALAGQ
691	6188	A	715	1	3552	
692	6189	B	716	1	3786	MVKGSIQQEELTILNIYAPNTGAPRF IKQVLSDLQRDLDSHTLIMGDFNNP LSTLDRSMRQKVNKDTQELNSALH QVDLDIYRTLHHKSTEYRFFSAPH HTYSKIDHILGSKALLSKCKRTEIT NYLSGHSIAIKLELKIKNLTQNRSTT

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						WKLNNLLLNDYWIHNEMKAEIKM FFETNENKDTTYQNLWDAFKAVCR GKFIALNAHKRKQERSKIDTLTSQL KELEKQEQTTHSKAGRKKEITKIRAQ LKEIETQKTLKMLNPGAEIQTIRE YYKHLIYAKKLENLEEMDKFLDTYT LPRLNQEEVESLNRPIGTAEIVAINS LPTKKSRTTRWIHSRILPEEASIIIPKP GRDTTKKENFRPISLMNIDAKILNKI LAKRIQQHIKKLIHHDQVGFIPGMQ GWFNIHKSINVIQHINRAKDKNHHIS IDAEKAFDKIQQPFMLKTLNKLIGD GTYFKIIRAIYDKPTANIILNGQKLE AFPLKTGTRQGCPLSPLLFNIVLEVL ARAIRQEKEIKGIQLGKEEVQLSLFA DEMIVYLENPIVSAQNLLKLISNFSK VSGYKINVQKSQAFLYTNNRQTES QIMSELPFTIASKRIKYLGIQLTRDV KDLFKENCKPLLNEIKEDTNKWNI PCSWVGRINIMKMAILPKVIYRFNAI PTKPPMTFFTELEKTTLKFIWNQKR ARIAKSILSQKNKAGGITLPDFKLYY KATVTKTAWYWYQNRDLQWNR TEPSEITPHIYSYLFDKPEKNKQWG KDSLFNKWCWENWLPICRKLKLDLP FLTPYTKINSRWIKDLNVRPKTIKTL KENLGITIQDIGMGKDFMSKTPKAM ATKDKIDKWDLIKLKSFCETAKETTI RVNRQPTKWEKIFATYSSDKGLISRI YNELKQIYKKKTNNPINKWVKDMN RHFSKEDIYAAKKHMKKCSSSLAIR EMQIKTTMRYHLTPLRMAIHKSGN NSASPTARNKTARNQRTKMIAVTA PRNRAPLELELILYRQNRQSKTHILE TNNTSAELLVPFEEDYLIEIRTVSDG GDGSSSEIRIPKMSMIDHILPKSIPE ELQNGEGFGYIMFRPVGSTTWSKE KVSSVSSSRFVYRNESIPLSPFEVK VGVYNNEGEGSLSTVTIVYSGEDD GYVFLWMVEPQLAPRGTSLSQSFSA SEMEVSWNAIAWNRNTGRVLGYE VLYWTDSDSKESMIGKIRVSGNVTT KNITGLKANTYFASVRAYNTAGTG PSSPPVNVTTKKSRYLITAYLEVPE I*
693	6190	A	717	2	3155	
694	6191	B	718	1	3414	MVKGSIQQEELTILNIYAPNTGAPRF IKQVLSLDLQRDLDSHTLIMGDFNNP LSTLDRSMRQKVNKDTQELNSALH QVDLIDIYRTLHHKSTEYRFFSAPH HTYSKIDHILGSKALLSKCKRTEIIT NYLSGHSIAKLELKIKNLTQNRSTT WKLNNLLLNDYWIHNEMKAEIKM FFETNENKDTTYQNLWDAFKAVCR GKFIALNAHKRKQERSKIDTLTSQL KELEKQEQTTHSKAGRKKEITKIRAQ LKEIETQKTLKMLNPGAEIQTIRE YYKHLIYAKKLENLEEMDKFLDTYT



SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						LPRLNQEEVESLNRPTGAEIVAINS LPTKKSRTTRWIHSRILPEVQGGTEK EGILPNSFYEASIIIPKPGRDTTKKE NFRPISLMNIDAKILNKILAKRIQQHI KKLIHHDQVGFIPGMQGWFNHKS NVIQHINRAKDKNHIIISIDA EKA FDKIQQPFMLKTLNKLGDGTYFKIIRA IYDKPTANIILNGQKLEAFPLKTGTR QGCPLSPLLFNIVLEVLAIRAEKE IKGIQLGKQEVQLSLFADEMIVYLE NPIVSAQNLLKLISNFSKVS GYKINVQKSQAFLYTNNRQTESQIMSELPFTI ASKRIKYLGIQLTRDVKDLFKENCK PLLNEIKEDTNKWKNI PCSWVGRIN IMKMAILPKVIYRFNAIPTKPPMTFF TELEKTTLKFIWNQKRARIAKSILSQ KNKAGGITLPDFKLYYKATVTKTA WYWYQNRDLQWNRTEPSEITPHI YSYLIFDKPEKNKQWGKDSL FNKW CWENWLPICRKLKLDPFLTPYTKIN SRWIKDLNVRPKTIKTLKENLGITIQ DIGMGKDFMSKTPKAMATKDKIDK WDLIKLSFCTAKETTIRVNRQPTK WEKIFATYSSDKGLISRIYNELKQIY KKKTNNPINKWVKDMNRHFSKEDI YAAKKHMKKCSSSLAIREMQIKTT MRYHLTPLRMAI KKS GNN SASPTA RNKTARNQRTKMIAVTAPNRAPL ELELILYRQNRQSKTHILETNNTSAE LLVPFEEDYLIEIRTVSDGGDGSSE EIRIPKMSTGEEGMAAVFKNKCRC SWSRVVIA YHSSSGNQMG TNPEQD PGQHAIPLEGTLTHTRTHSDWDHLD TAMN*
695	6192	A	719	1	5127	
696	6193	A	720	965	9275	
697	6194	A	721	3	376	
698	6195	A	722	1	380	
699	6196	A	723	104	462	
700	6197	A	724	762	902	
701	6198	A	725	78	747	LRRGRSRETNEEPPPTVQVQGGPGP QREEKQKTKMAKFVIRPATAADCS DILRLIKELAEY EYMEEQVILTEKDL LAEDGFG\ EHPFYHCLVAEVPKEHW TSEG\HSIV\GFAM\YYFTY\DPWIGQ VICILEDFF\VM\SDYRGSIGSEIL\K\NLSQ\VAMRCRCSSMHFLG*PEWVN EPS\NFY\KRRGAS\DLSS*RRGWRL FQGS DKGVIWLKNGPTEGVEGVAC C
702	6199	A	726	149	460	
703	6200	A	727	1	501	
704	6201	A	728	1	391	SPLNKVQLINELNEREVQLGVANK VSWHSEYKDSAWIFLGGLPYDLTK GDIICVFSQ\QRSTIVA VDNFN GIKIKGRTIRVDHVSNYRAPKDSEEID DVT RQLQEKGC GARTPSPSLSESSEDEK

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						PTKKP
705	6202	A	729	18	240	
706	6203	A	730	254	1223	SPLTRVKLINELNEREVQLGVADKV FWHSEYKDSA WIFLGGLPYGLT\EG DIICVFSQYGEIVNINLVRD\KKTGK SKGFCFLCYEDQRSTILAVDNFNGI KIKGRTIRVDHVS\NYRAPKDSIEDID DVTRQLQEKGGSGARPPSPPTLSESSE DEKPTKKHKKDKK\EKKKKKKEKE KADREVQAEQPSSSSPRRKTVKEKD DTGPKKHSSKNSERAQKSEPREGQ KLPKSRTAYSGGAEDLERELKKEKP KHEHKSSSRREAREEEKTRIRDRGRS SDAHSSWYNGRSEGRSYRSR SR DKSHRHKRARRSRERESSNPSDRW RH
707	6204	A	731	2143	2346	
708	6205	A	732	2016	2206	
709	6206	A	733	90	401	
710	6207	A	734	276	488	
711	6208	A	735	186	537	IWFPLRRRKARQEEKSGLGAPRSPS HNYPGPGYLGCLGKTNTS*TYILDQS NIGKRVA\AILN*ILGGRKLRLKSL SCQPKVEELYERVAW/IP*KPGCLLL VSVKVRNVFDWCTWVY
712	6209	A	736	3	318	
713	6210	A	737	1	280	REPTMVLSPADKTNVKA AWGKVG AHAGEYGAEALERMFLSFPTTKT\P VNFKLLSHCLLV\TLAAHLPAEFTPA VHASLDKFLGSVSTVLT SKYR
714	6211	B	738	34	264	MVLSPADKTNVYFPHFDLSHGSAQ VKGHGKKVADALTNAV RTVDDMP NALSALSDLHAHKLRVDPVNFKLL STACW*
715	6212	A	739	3	190	EPTMVLSPADKTNVKA AWGKVG H/AGEYGAEALERMFLSFPTTKIQIP LSWSLGGHASCPLG
716	6213	B	740	12	298	MVLSPADKTNVKA AWDL PALRPE PRLCQVKGHGKKVADALTNAVAH VDDMPNALSALSDLHAHKLR LAW*
717	6214	A	741	2	392	QTQREPTMVLSPADKTNVKA AWG KVG AH/AGEYGAEALERMFLSFPTT KTYFPHFDLSHGSAQVKGHGKKVA DALTN AV/AHVGGPVNFKLLSHCLL VTLAAHLPAEFTPAVNASLDKFLV SVSTVLT SKYR
718	6215	A	742	623	1235	SNLVELSNTLSWSSGGKVG AHAGE YGAEALERMFLSFPTTKTYFPHFDL SHGSAQVKGHGKKVADALTNAVA HVDDMPNALSALSDLHAHKLRVDP VNF\KLL\SH\CLLVDPGPAHFPAEF\ TPAVHASLDKSTKTYFPHFDLSHGS AQVKGHGKKVADALTNAVAHVDD MPNALSALSDLHAHKLSVDPGNFK LPSHLPAGDPC
719	6216	A	743	117	403	
720	6217	C	744	62	370	MKSMRKQAPIITAFILTSRSGNWIP

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						KLSASVNASLKIPVQCLEILPTTHCS SRDLIFQKFNLLMNQYLIYLGMLSV DTEEDTQLASLFPGEKHSSVSFVCP*
721	6218	A	745	3	1242	AAPQAGLSPVAIAAAIQLHLHSTQC SSPNTCCLP RRTRATIYYSRWSYHP LGSVP*SP*PFQEAS/ALTLPPACSFY GPLT*FQPKP*GSFPLSQ*MEYTIGL YT*TFHCPGTSRRQIPSSYL NCKDAF LPLL/SNPPQCRPFTGVGLVDVLTGF ETNNKYEIKNSFGQRVYFAAEDTD CCTRNCCGSPRPFTLR IIDNMGEVI TLERPLRCS SCCCPCCLQEIKSLDEQ CVVGKISKYWTGILREAF TDADNFG IQFPLDL DVKMKA VMIGACFLIDRN CSPAMEQSWMENYFDEMTEIGFRR SVITNFSELKEHVLTHCKEANKNLD KMLDEWLTRKNSVEKTLNELMEV KTINEKLTIGKISKYWSGFVNDVFT NADNFGIHVPADLDVTVKAAMIGA CFLFAFRLGSELHN
722	6219	A	747	129	1235	EGCAAAVPDSLEAQKRKPSPGGSL DLVSLGSGNSGSQRTVLIMDKQNS QMNASHPETNLPVGYPPQYPPTAFQ GPPGYSGYPGPQVSYP PPAHSGP GPAGFPVPNQPVYNQPVYNQPVGA AGVPWMPAPQPPLNCPGLEYSQI DQILIHQQIELLEVLTGFETNNKYEI KNSFGQRVYFAAEDTD CCTRNCCG PSRPFTLR IIDNMGEVITLERPLRCS SCC\CPCCLEIEIQAPGPVIGYVIQ TWHPCLPKFTIQNEKREDVLKISGP CVVCSCCGD VDFEIKSLDEQCVVG KISKHWTGILREAF TDADNFGIQFP LDLDV KMKA VMIG\ACFL\DFMFF\ ESTGQPGNKNSGVWVVGFS
723	6220	A	748	647	797	
724	6221	A	749	2	424	
725	6222	A	750	2	460	ARAHTHREPTMVLSPADKTNVKAA WGKVG AHAGEYGAEALERM LLSF PTTPTYFPHFDLNHGS AHVKGHGK NVDDALTNAVTHVYYMPNSLYALS DLHPHNL RMDPVNFMLLSHCLL*T LVVHLPAELTPAVHASLNNVLESER TELTSSTS
726	6223	A	751	1	456	RPRRPQREPTMVLSPADKTNVKAA WGKVG AHAGEYGAEALERMFL/SF PTTKTYFPHFDLSHGSSQVKGHGKK VADALTNAVGHVDDMPNALSALS DLHAHKL RVDPVNFKLLSHCLLVT LAAHLPAEFTPAVHAFLDKFLASVS TVLT SKYR
727	6224	A	752	1	594	PRLFWSPQTQREPTMVLSPADKTN VKA AWGKVG AHAGEYGAEALER MFLSFPTTKTYFPHFDLSHGFAQVK GATGKKVDD\ALTKRRGAPLDGMP NALVRPLKRPCTTHKAFGVPEGSTS KLL\SHLPCLGEPWAAHLPRPSFNP WRLQRLPWGQSFLGFLVEEPLLEPS

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						KIPVKAWKPSVGHCCFFAPWGFPPAPSSLS
728	6225	A	753	2	386	
729	6226	A	754	33	476	
730	6227	A	755	5	417	
731	6228	A	756	1	412	
732	6229	A	757	2	446	
733	6230	A	758	3	713	
734	6231	A	759	87	236	
735	6232	A	760	181	322	
736	6233	A	761	213	427	
737	6234	A	762	213	422	
738	6235	A	763	1	732	
739	6236	A	764	31	1074	TLILSGFTVKQVY AIDQIFSSLRLTIT IKMFCGDYVQGTIFPAPNFPNIMDA QMLGGALQGFDCDKDMLINILTQR CNAQRMMIAEAYQSMYGRDLIGD MAREQLSDHFQDVMAGLMYPPPLY DAHELWHAMKGVGTDENCLIEILA SRTNGEIFQMREAYCLQYSNNLQE DIYSETSGHFRDTLMNLVQGTREEG YSDPAMAAQDAMVLWEACQKKTG GHKTM LQMILCNKSYQQLRLVFQE FQNISGQDMVD AINECYDGYFQELL VAIVLCVRDKPAYFAYRLYSAIHDF GFHNKTVIRILIARSEIDLLTIRKRYK ERYGK\SLFHDIRNF\ASGHYKKGSTG LPIC
740	6237	A	765	613	926	
741	6238	C	766	79	405	MIGGTPQMFFISGAKGQWSPSLQPP PRAHRSSPWAPSSKSTSGGTAALGS LGSKDYFPRGTG DGVVELRRSDQRR AHLPGCPTVLR TLLPQQRGDRDLQ QLRHHELRL*
742	6239	A	767	1	321	
743	6240	A	768	110	431	
744	6241	B	769	756	1533	MREIVHIQAGQCGNQIGAKFWEPW KASSIELSQCRNSPSKVFRSKEHDGL PVTPTTR*
745	6242	A	770	20	453	GIPGSTISLFCSEKKLREVERIVKAN DREYNEKFQYADNRIHTSKYNILTF LPINLFEQFQRVANAYFLCLLILQLI PEISSLTWFTTIVPLVLVITMTAVKD ATDD\ILQNEKWMNVKVGDIKLEN NQFVAADLLLLSSSEPH
746	6243	A	771	1	1014	
747	6244	A	772	128	2654	LVQDHKAGEHQVGAMARLGNC SL TWAALIILLPGSLEECGHISVSAPIV HLGDPITASCIKQNC SHLDPEPQIL WRLGAELQPGGRQQR LSDGTQESII TLPHLNHTQAFLSCCLNWGNSLQIL DQVELRAGYPPAIPHNLSCLMNLTT SSLICQWEPGPETHLPTSFTLKSFKS RGNCQTQGDSILDCVPKDGQSHCCI PRKHLLLYQNMGIWVQAENALGTS MSPQLCLDPMDVVKLEPPMLRTMD PSPEAAPQAGCLQLCWEPWQPGL

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						HINQKCELRHKPQRGEASWALVGP LPLEALQYELCGLLPATAYTLQIRCI RWPLPGHWSWSPSLELRTTERAP TVRLDTWWRQRQLDPRTVQLFWK PVPLEEDSGRIQGYVVSWRPSGQAG AILPLCNTTELCTFHLPSAEQVAL VAYNSAGTSRPTPVVFSESERGPALT RLHAMARDPHSLWVGWEPPNPWP QGYVIEWWGLGPPSASNSNKTWRME QNGRATGFLLKENIRPFQLYEIIIVTP LYQDTMGPSQHVVAYSQEMAPSH APELHLKHIGKTWAQLEWVPEPPEL GKSPLTHYTIFWTNAQNQSFSAILN ASSRGFVLHGLEPASLYYHIHLMAAS QAGATNSTVLTLMTLTPEGSELHIL GLFGLLLLLTCLCGTAWLCCAPTG RIPSGQVSQTQLTAAWAPGCPQSW RSCPDPRDSGWGRHLK*AVLSPHI LVCRMPSSCPALARHPSPPSQCWRR MKRSRCPGSPITAQRPVASPLWSRP MCSRGTEQFPPSPNPSLAPAIRSFM GSCWAAPQAQGGGTISAVTPLSPS WRASPPAPSPMRTSGSRPAPWGPW
748	6245	A	773	123	2486	
749	6246	A	774	128	2573	LVQDHKAGEHQVGAMARLGNCSL TWAALHILLPGSLEECGHISVSAPIV HLGDPITASCIKQNCSHLDPEPQIL WRLGAELQPGGRQQRLSDGTQESII TLPHLNHTQAFLSCCLNWGNSLQIL DQVELRAGYPPAIPHNLSCLMNLTT SSLICQWEPGPETHLPTSFTLKSFKS RGNCQTQGDSDLCVPKDQGSCHCI PRKHLLLYQNMGIWVQAENALGTS MSPQLCLDPMDDVVKLEPPMLRTMD PSPEAAPPQAGCLQLCWEPWQPG HINQKCELRHKPQRGEASWALVGP LPLEALQYELCGLLPATAYTLQIRCI RWPLPGHWSWSPSLELRTTERAP TVRLDTWWRQRQLDPRTVQLFWK PVPLEEDSGRIQGYVVSWRPSGQAG AILPLCNTTELCTFHLPSAEQVAL VAYNSAGTSRPTPVVFSESERGPALT RLHAMARDPHSLWVGWEPPNPWP QGYVIEWWGLGPPSASNSNKTWRME QNGRATGFLLKENIRPFQLYEIIIVTP LYQDTMGPSQHVVAYSQEMAPSH APELHLKHIGKTWAQLEWVPEPPEL GKSPLTHYTIFWTNAQNQSFSAILN ASSRGFVLHGLEPASLYYHIHLMAAS QAGATNSTVLTLMTLTPEGSELHIL GLFGLLLLLTCLCGTAWLCCAPTG RIPSGQVSQTQLTAAWAPGCPQSW RRMPSSCPALARHPSPPSQCWRRM KRSRCPGSPITAQRPVASPLWSRPM CSRGTEQFPPSPNPSLAPAIRSFMG SCWAAPQAQGGGTISAVTPLSPSW RASPPAPSPMRTSGSRPAPWGPW
750	6247	A	775	151	273	

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751	6248	A	776	785	920	
752	6249	A	777	332	473	
753	6250	A	778	264	387	
754	6251	A	779	257	354	
755	6252	A	780	101	290	
756	6253	A	781	21	215	
757	6254	A	782	158	955	KMTSSSEQEEDEKNNQSATPRQTGP ATTMNSKGQYPTQPTYPVQPPGNP VYPQTLHLPQAPPYTDAPPAYSELY RPSFVHPGAATVPTMSAAPG\ASL YLPMAQ\SVAVGPL\GSTIPMAYYP VGPIYPP\GST\VLGGKGGYDAGARF GAGATAGNIPPPPPG\CPPNAAQLA VMQGANVLVTQ\RKGNFFMGGS DG GYTHLVRNQGHLCAREKTSHTLQH FSQCNCFSHINLKLQFRHMLLGCLS GAQTRHFSNLIRNHVMVAVPP
758	6255	A	783	167	342	
759	6256	A	784	368	525	
760	6257	A	785	311	487	
761	6258	A	786	148	298	
762	6259	A	787	164	314	
763	6260	A	788	232	382	
764	6261	A	789	2	390	
765	6262	A	790	3	376	AQKAGLGTIFIMTCSPLLLTLLIHCT GSWAQPVLTQPPSVSAAPGQKVTIS CSGSGSNIGNNYVSWYQQLPDPLFH AHK*LLPGSRDSGLEAR*QPRQGGS GDHHTLQTKQQQVRGQQLPEPDA
766	6263	A	791	2	353	
767	6264	A	792	2	382	
768	6265	A	793	3	654	
769	6266	A	794	9	885	
770	6267	A	795	1	412	
771	6268	A	796	2	616	WPIEIDIQCGGIPRDNLHHDLLPSP HPSHCPTRPAVSAEGRTRDQSSSM TCSPLLLTLLIHCTGPWAQSVLTQPP SVSATPGQRTVISCGRSRSNIGDNYV SWYKQLPGTAPQLLIYDNNKRTSGI PDRFSGSKS\GTSATLGITGLQTGDE ADYYCGTWDITLSAGVFGGWTKLT VLGQPKAAPSVTLFPPSSEELQANK AT
772	6269	A	797	489	715	
773	6270	A	798	20	371	
774	6271	A	799	181	382	
775	6272	A	800	353	479	
776	6273	A	801	3	368	HEAASSSSASPFQTKIEKMVDLTQV MDDEVFMAFASYATIILSKMMLMS TATAFYILTRKVFNAPQHCVTFGKG ENAKKYLRTDDRVR*VRRRAHLNDL ENIIPFLGIGLLYSLSGADPSTAI
777	6274	A	802	246	363	
778	6275	B	804	55	366	MGHFTFEEDKATITSLWGKVNVEDA GGETLGRLLVVYPWTQRFFDSFGN LSSASAIMGNPKVKAHGKKVLTSL GDAIKHLDDLKGTFAQLPHRLVIVA

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						LSSSVK*
779	6276	A	805	129	409	
780	6277	A	806	24	253	
781	6278	A	807	32	433	
782	6279	A	808	15	468	
783	6280	A	809	25	1404	APSPDAMGHFTEEDKATITSLWGK VNVEDAGGETLGRLLVVYPWTQRF FDSFGNLSSA\SAIMGNPVKVKAHGK KVLTSLGDAIKHL\DDLKGTFAQLE *TCTCDKL\H\VDPENFKLLG\NVLV TVL\AIHF\GKEFTPE\VQSFLGRKMV TGVASALSFPDYH
784	6281	A	810	113	387	
785	6282	A	811	1330	1465	SECCGLSRPGHWPFI*WLPSL/CLI DVPT*QRKGGLVRNWVLP*NLWE LLP/ALAGSGEGHLKNMTGSKLSRM PNRISDSESE/GVNTARIHGEMFWR GDNWACTCCRGARLSAADSADPA TGLTSFPLASASSSATRASIPKRCLN SWFSTTRP
786	6283	B	812	17	718	MVVVAAAPNPADGTPKVLLLSGQP ASAAGAPAGQALPLMVPAQRGASP EAASGGLPQARKRQRLTHLSPEVPS LPRKLKNRVAAQTARDRKARMSE LEQQVNQKLLLENQLLREKTHGLV VENQELRQRLGMDALVAEDFCLLQ SDILLGILDNLDPVMFFKCPSPEPAS LEELPEVYPEGPSSLPASLSLSVGTS SAKLEAINELIRFDHIYTKPLVLEIPS DTG*
787	6284	A	813	464	714	
788	6285	A	814	349	581	
789	6286	A	815	223	513	DHEEPQAREGDQSVHRPHAERTGQ PGMWRHPRLDECQPQELL/TKHSTS PSQEKEVHTPHP/RPLESCWASLNR DPQHSSPTPGKTSKRENIISQ
790	6287	A	816	384	464	PLPQLLRFAQPKPEAHLTPARPQPK RTCHGLTCRRGVSPGWRRDGPWRT HRSAGATRRPIQETASVPQPEAAPP HRARGSGKMRDGKPGAGNTERRD PQSRTVGLNKKNSTPHQSPQPPADV *TSAGG
791	6288	A	817	1	255	IVMGHSMLPHF*IWSPPPGRAAARL APLSGAGHSGPRLAPWT*AGQLQT QSLVR/P*PELGKSELSAPSLVIGSW MDM*PKPGQ
792	6289	B	818	191	1072	MWRSLRLRXRGTPSPESAGGWPQ RFYESGANHPVSSPGLRPADRKEEV LFRMFSIHTGEALAIAVATEWDSQQ DTIKYYTMHLTTLCNTSLDNPTQRN KDQLIRAAVKFLDTDITICRYVEEPE TLVELQRNEWDPHIEWAEKRYGVEI SSSTSIMGPSIPAKTREVLVSHLASV NTWALQGIDGSRPCCCSRLEEEYQI PEVGGNIEWAHDYELQELRARTAA GTLFIHLCSESTTVKHKLLKE*
793	6290	A	819	1518	1891	

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794	6291	A	820	217	491	
795	6292	A	821	1789	2411	KTYWRKKVEKVVVSNR\LTSPC\C IVTSTYGWTANMGENH*KLQALKE TTSTMG/YMASQRKHRGKPLTSLI IEYLKAKRPEGLIRTDKS\VKDL\VIL LYETALLSSGFQSWKIPRHH*QVS YRMIKL\GLGIDEDGPYLLDDTSA\A VNLKELPP\LEGDDDTFTHGKEVGLI LLGLRGWTLPVSVLYNSSDNIFFQG CFPLFLVNI
796	6293	A	822	592	1122	
797	6294	A	823	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFDFSFGNLSSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLVTVAIHFGKEFTP EVQASWQKMVTGVASALSSRYH
798	6295	A	824	38	531	APSPDA\MGHFTEEDKATIT\SLWGK VNVE\DAGGETLGRLLVVYPWTQR FFD\SFGNLSSASAIMGNPKVKAH GKKVLTSLGRCHKSTWDDLKG\TF AQA*SELHL*QSCNVDPENFKLLG\ NVLVTRFGQSHFRQKNFTPEGCRAS WAE/MMGDLQLASALVPSRYH
799	6296	A	825	1	278	
800	6297	A	826	80	591	RGCKREGLSMSSLIRRVISTAKAPG A\IGPPTVQAVLV\DRTHLHFRDQIG HGPLPSWTS\CPGGVAGRSLNKL KNMGEIPESLPGCDFTNVVKTTCS GLDINDLQLLFNEILQTVFSRSNFP RAAYPSWLLLPQKGSRIEIA\VAIQ GPLTTAFILSGDPCCVWDC
801	6298	A	827	1	396	
802	6299	A	828	1	346	
803	6300	A	829	3	720	RGIPASRWARKAVVLLCASDLLLLL LLLPAG\SGRAEGSPGTP\DEFTP\PP RKKKKDIRDSNDADMARLLEH\WE KHDD\EEGDLPEHKRPSAPVDFSKI DPG\KPESILKMTKKGKTLMMFVT VSGSPTEKETEEITSLWQGS\LFNAN YDVQRFIVGSDRAIFMLRDGSYAW EIKDFLVGQDRCADVTLEGQVYPG KGGGSKEKNKTKQDKGKKKKEGD LKSRSKEENRAGNKREDL
804	6301	A	830	349	567	
805	6302	A	831	1098	1684	
806	6303	A	832	2	441	PCRNRSVENFVSMWVCSTLWRVRT PPGSG/GLLPASGCHGPAASSYSA SAEPARVRALVYGHGDPKVVET VIPGHTWQLRNVA*PTLRR*FERNT HSSLDDMNISVWLCA*\LKNLELAA VRGSDVRVKMLAAPINPSDINMIQG
807	6304	A	833	3	421	ASMWVCSTLWRVRTPPGSG/GLL PASGCHGPAASSYSASAEPARVRAL VYGHGDPKVVVEGITRELFQRF WIFLQLITAVISSASTVLKNLELAAV RGSDVRVKMLAAPINPSDINMIQGN



SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						YGFLPELPAVGGNEGV
808	6305	A	834	2	611	ILQLGRGRAVRVCSTLWRVRTP\PG SGG/GLLPASGCHGPAASSYSASAEP ARVRALVYGHGDPKVVVELKNL ELAAVRGSDVRVKMLAAPINPSDIN MIQGNYGLLPELPAVGGNEGVAQV GAEGSNVTGLKPGNWVVP\NAGL RTWRNRG*VHPKEALIQVPSDIPLQ SAATLGVNPCTAYRMLMDFEQLQP GDSVIQNAS
809	6306	A	835	159	312	
810	6307	A	836	637	974	
811	6308	A	837	240	419	
812	6309	A	838	20	283	
813	6310	A	839	508	715	IPGNFEPSRLGRG*KTQACSPSLLWE FWLTQYLPALGAGHILKNFTTFPVI\ SCVSKLSTLFGGKMPEN
814	6311	A	840	3	362	
815	6312	A	841	7	479	GAIMGVDIANKDRRVRRKEPKSQD IYLRLLVKLYRFLARRTNSTFNQVV LKRLFMSRTNRPLSLSRMIRKMKL PGRENKTAVVVGTITDDVRVQVEP KLKVCALRVTSRARSRLRAGGKIL TFDQLALD\SPYVRSGRKFERRARG RRASRGYKN
816	6313	A	842	2	723	CAVNSAEQRGAIMVSGHLFITKDRK VR\RKEPKSDIYLRLLVKLYRFLA RRTNSTFNQVVLKRLFMSPHQPGP PLSL\RMIPED*SFPGPQKQRRVAVV VG\TITD\DVVRVQEV\VPKTERVCCTC AVDQAGAPQAAILRAGGQDSFTFR PSLALGTSPKGLVGTCSWLFRFPQ RGPRRWYPAIFGKGPGQGTAPAQATP KPYV\RSKGPKFERARG\RRAS\RGY KKLTLDPTLLLKKFLPDKKK
817	6314	A	843	1221	2238	EPLIVCVCFFCLCPPLFFFSFLGSAEK AVLEQFGFPLTGTEARCYTNHALSY DQAKRVP\RWVL\EHIFQKAR*\MG DADRKHCKFKPDNPITTFSAFNEN YVGSGWSRGHMAPAGNNKFSSKA MAETFYLSNIVPQDFDNNSGYWNRI EMYCRELTERFEDVWVVSGLTLPL QTRGDGKKIVSYQVIGEDNVAVPS HLYKVILARRSSVSTEPLALGAFVV PNEAIGFQPQLTEFQVSLQDLEKLS VLVFFPHLDRSTDIRNICSVDTCCLK DFQEFTLYLSTRKIEGARSVLRLEKI MENLKNAEIEPDDYFMSRYEKKLE ELKAKEQSGTQIRKPS
818	6315	A	844	1	306	
819	6316	A	845	216	339	
820	6317	A	846	425	553	
821	6318	A	847	190	334	
822	6319	A	848	241	435	
823	6320	C	849	280	450	MLEKNWCPSLQVPIILNWAQPCGKI LTECCTLGYSLIQGDFWTFIRKHAR TRLVKR*

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824	6321	A	850	1	301	
825	6322	A	851	2	3484	
826	6323	B	852	225	326	MAFKDTGKTPVEPEGAIHRIRITLTS RKRKSFEK*
827	6324	A	853	348	515	AFKDTGKTPVEPELAIHRI\IRITLTS\ RNVKSLEK\VSASFVMRGGGGIGRK ATSFTR
828	6325	A	854	42	529	SARSLHDSPHVRSRRGTSVRKPA RNRPLAFKDT\GKTPVEPEV\AIHRI RITPNKAA\NVK\SLEKVVCLTLIRRA QKEKNFQS*KGPVS/RLPYPRFLRIH FQGKTPCGLKVFKDVGVRFPWRRI HK\RL\LDLHSPSIEIVKQITFHQYLSP GVEVEVHHLQML
829	6326	A	855	14	345	
830	6327	A	856	1	396	
831	6328	A	857	3	718	RGIPASRWARKAVVLLCASDLLLLL LLLPPAG\SGRAEGSPGTP\DEFTPPP RKKKKDIRDSNDADMARLLEHWE KHDD\VEGDLPEHKRPSAPVDFSKI DPSKPESILKMTKKGKTLMMFVTV SGSPTEKETEEITSLWQ\SLFNANY DVQRFIVGSDRAIFMLRDGSYAWEI KDFLVGQDRCADVTLEGQVYPGKG GGSKEKNKTKQDKGKKKEGDLK SRSSKEENRAGNKREDL
832	6329	A	858	80	349	
833	6330	A	859	504	738	
834	6331	A	860	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSSA SAIMGPNPKVKAHGKKVLTSLGDAI KHLDDLKGTFQALSELHCDKHLHVD PENFKLLGNVLVTVLAIHFGKEFTP EVQASWQKMTGTVASALSSRYH
835	6332	A	861	38	608	APSPDA\MGHFTEEDKATITSLWGK\ VNVE\ DAGGETLGRLLVVYPWTQR FFD\SGNLSSASAIMGNPKVKAH GKKVLTSLGDAIKHLDDLKGTFQ L\SELH\CDK\HVDPENFKLLGEML LTVV\LAIPFRAKEFTPEGCRASWQ KQKMAEDGDLQWPSGPVPPDTTEA SWPMNSEAFKDKAFILASNYK
836	6333	A	863	727	1089	
837	6334	A	864	432	742	
838	6335	A	865	184	352	
839	6336	A	866	204	394	
840	6337	A	867	1	2286	MDLLGRVGS DWALQSSCLTDP ELW GWEGTPRFLAAAAQGFGGPVLKAQ ACSLGAGIAPTELPRPVRWSLLFLA VRSNYQALWPQSPAGLPLVPQPETP RGANIPSPV VVHAGDDR GWHMTV EQKFGLFSAEIKEADPLAASEASQP KPCPPEVTPHYIWIDVRACSPKAV GCSTWGARTVPGVGVAEPKAFGKL GQSAQNPSA VSAGPRFLVQRFEIA KYCSDQVEIFSSLLQRSMSLNIGRA KGS MNRHVAAIGPRFKLLTLGLSLL

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						HADVVPNATIRNVLREKIYSTAFDY FSCPPKFPTQGEKRLREDISIMIKFW TAMFSDKKYLTAQLVPPADIGDLL EQLVEENTGSLSGPAKDFYQREFDF FNKITNVSAHKPYPKGDERKKACLS ALSEVTVQPGCSLPSNPEAIVLDVD YKSGTPMQSAAKAPYLAKFKVKRC GVSELEKEGLRCRSDSEDECSTQEA DGQKISWQAAIFKLGDGCRQDMLA LQIIDLFKNIFQLVGLDLFVFPYRVV ATAPGCGVIECIPDCTSRDQLGRQT DFGMYDYFTRQYGDESTLAFQQR YNFIRSMAYSLLLFLLQIKDRHNG NIMLDKKGHHIHDFGFMFESSPGGN LGWEPDIKLTDEMVMIMGGKMEA TPFKWFMEMCVRGYLA VRPCLGST GDRVQQIESCLGDVQDVAGEAYM DVVVSLVTIMLDTGLPCFRG/QIKFL KHRFSPNMTEREAA NFIMKVIQSCF LSNRSRTYNMIQYYQNDIPY
841	6338	A	868	3	164	
842	6339	A	869	1	5340	
843	6340	A	870	649	1028	
844	6341	B	871	1	5823	MCPVDFHGFQDLERRRDAVIALGI FLIESDLQHKDCVVPYLLRLLKGLP KVYWVEESTARKGRGALPVAESFS FCLVTLLSDVAYRDP SLRDEILEVLL QVLHVLLGMCQALEIQDKEYLCKY AIPCLIGISRAFGRYSNMEESLLSKL FPKIPPHSLRVLEELEGVRRRSFNDF RSILPSNLLTVCQEGTLKRKTSSVSS ISQVSPERGMPSPSPGGSFAHYFEA SCLPDGTALEPEYYFSTISSFSVSPL FNGVTYKEFNIPLEMLRELLNLVKK IVEEAVLKSLDAIVASVMEANPSAD LYYTSFSDPLYLTMFKMLRDTLYY MKDLPTS FVKEIHDFVLEQFNTSQG ELQKILHDADRIHNEL SPLKLRCQA SAACVDLMVWAVKDEQGAENLCI KLSEKLQSKTSSKVIIAHLPLLICCL QGLGRLCERFPVVVH SVTPSLRDFL VIPSPVLVKLYKYHSQYHTVAGNDI KISVTNEHSESTLNVMSGKKSQPSM YEQLRDIAIDNICRCLKAGLTVDPI VEAFLASLSNRLYISQESDKDAHLIP DHTIRALGHIAVALRDT PKVMEPI QILQQKFCQPPSPLDVLIIDQLGCLVI TGNQYIYQEVWNL FQQISVKASSV VYSATKDYKDHGYRHCSLAVINAL ANIAANIQDEHLVDELLMNLEL FV QLGLEGRASERASEKGPALKASSS AGNLGVLPVIAVLTRRLPPIKEAKP RLQKLF RDFWLYSVLMGF AVEGSG LWPEEWYEGVCEIATKSPLLTFPSK EPLRSVLQYNSAMKNDTVTPAELSE LRSTIINLLDPPPEVSALINKLDFAM STYLLSVYRLEYMRVLRSTDPDRFQ VMFCYFEDKAIQKDKSGMMQCVIA

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						VADKVFDFAFLNMMADKAKTKENE EELERHAQFLLVNFNHHKRIRRVA DKYLSGLVDKFPHELLWSGTVLKTM LDILQTLSSLADIHKDQPYDIPD APYRITVPDYEARESIVKDFAARC GMILQEAMKWAPTVTKSHLQEYLN KHQNWVSGLSQHTGLAMATESILH FAGYNKQNTTLGATQLSERPACVK KDYSNFMASLNLNRNRYAGEVYGM RFSGTTGQMSDLNKMVMVQDLHSA LDRSHQPQHYTQAMFKLTAMLISSK DCDPQLLHHLWCWGLRMFNEHGM ETALACWEWLLAGKDGVEVPFMR EMAGAWHMTVEQKFGFLSAEIKEA DPLAASEASQPKPCPEVTPHYIWD FLVQRFEIAKYCSSDQVEIFSSLLQR SMSLNIGGAKGSMNRHVAAIGPRF KLLTLGLSLLHADVVPNATIRNVLR EKIYSTAFDYFSCPPKFPTQGEKRLR EDISIMIKFWTAMFSDKKYLTASQL VPPDNQDTRSNLDITVGSRRQATQG WINTYPLSSGMSTISKSGMSKKTN RGSQHLHKYYMKRRTLLLSLLATEIE RLITWYNPLSAPELELDQAGENSVA NWRSKYISLSEKQWKDNVNLAWSI SPYLAVQLPARFKNTEAIGNEVTRL VRLDPGAVSDVPEAIKFLVTWHTID ADAPELSHVLCWAPTDPTGLSYFS SMYPPHPLTAQYGVKVLRSFPPDAI LFYIPQIVQALRYDKMGYVREYILW AASKSQLLAHQFIWNMKTNIYLDE EGHQKDPDIGDLLDQLVEEITGSLS GPAKDFYQREFDFFNKITNVSAHKP YPKGDERKKACLSALSEVKVQPGC YLPSNPEAIVLDIDYKSGTPMQSAA KAPYLAKFKVKRCGVSELEKEGLR CRSDSEDECSTQEADGQKISWQAAI FKVGDDCRQDMLALQIIDLFKNIFQ LVGLDLFVFPYRVVATAPGCGAIEC IPDCTSRDQLGRQTDGMYDYFTR QYGDESTLAFQQARYNFIRSMAY SLLLFLQSKDRHNGNIMLDKKGHI IHIDFGFMFESSPGGNLWEPRHQA DG*
845	6342	A	872	1	337	
846	6343	A	873	1	337	
847	6344	A	874	838	929	
848	6345	A	875	21	338	
849	6346	A	876	2	424	
850	6347	A	877	3	452	
851	6348	A	878	3	604	PTLLVPTDSERTHPWLLSPADK\TN VKA\AWGKVGAGHAGEYGAEALER MFLSFPTTKTYFPHFDLSHGSAQV\ KGGH\KKVADALTNAVAHV\DDMP N\ALSALSDLHAHKL\RVGPGSTFKL LK\HTCLAGEPWAAHLP\AEFQPLA VATSSLGTFKPGLLVEAPLLTFQIPV KAGSLGWPLFFCPLGLPPSPSPFLH

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						PYPRGL
852	6349	A	879	2	416	EGKPRTS GA EHR SCRGKAS MSPNF KLQCHFILIFLTALRGESRYLELREA ADYDPFLFSANLKRELAGEQPYRR ALRCLDMLSLQGQFTFTDDRPQLH CAGFFISEPEESLPFHYDQ*SIDGK AGNFLKVL MGRIL
853	6350	A	880	1	187	
854	6351	A	881	2	1099	PRVVRGRV GEGVGRKAQDLRSRQHS SCRGKAS MSPNFKLQCHFILIFLTAL RGESRYLELREAADYDPFLFSANL KRDVAGEQPYRRALRCLDMLSLQG QFTFTADRPQLHCAAFFISEPEEFITI HYDQVSI GLSKGGDF/LWKVFDGWI LKGEKFP\SSQ\DHPLPSAERYIDF\C ESGLSRRSIRSSQNV\AMIFFRVHEP GNGISHLTIKTDPNLFSFAMFISSEFQ MGKFNLG*FPHQHRNCSFSIYPV\VI KISDLYPGGHVNGSFS*RKSS\AGCE GIGDFVELLGGTGLDPSKMTPLADL CYPFHGPAQMKVGCDNTVV\RMVS SGKHVN RVDFLRIVQLEAVTSWEN PNG\NSIGEFCLSGL
855	6352	A	882	2	645	HGIQAHGQIPSYKTIGGRDDSFHTFF SETGAGKHVPRLLL*NWKPTVMDE VRTGTYCQLFHLEQFITARKIAANN YARGHYTIGKEIIDLVLDRIKRLAD QCTGLQGFLVFHSFGGGTGSGFTSL LMERLSVDYGKSKLEFSIYPAPQV STAVVEPYNSILTHTTLEHSDCAF MEEGEFSEAREDMAALEKDYEEVG VDSVEGEGEEEEGEY
856	6353	A	883	90	1657	EATTSPLRLRHQLGSREAATMRECI SIHVGGQAGVQIGNACWELCYLEHGI QPDGQMPK*PKPLGEGDDSFNTFFS ETGAGKHVPRAVFVDLEPTVIDEVR TG\TYRQLFHPEQLITGKEDAANNY ARGN\YTIGKEIIDLVLDRIKRLA\DQ CTGLQGFLVFHS\FGGG\TGSGFTS\ LLMERLSVDYWQESPSLEFSIYPAA PRFPQPVVEP\YN\SILPTQHPPWEHS DCAFM\VDNEAIYDICRRNLDIERP TYTNLNLRL\ASQIVSSITASLRFDGAL NVDLTNEFQTNLG\PYPPIHFP\ATY APCHLC*RKPTHEQLFCSQRSPKCF AFEPTNPDG*NGDPR\HG*IHWLAC LLLP/RGDVVPKRCQMLPIAHPKSKP KRS\IQFVDWCP\TGFKV\GINYQPP\ TVVPGGDLA\KV TREAVCMLSKHH SPFAEAWARPGPTSF DLM LCQACPF VHWYLG\EGMEEGEFSK\ARKDMA AL\RKDYEEVG\VDSVKG\EGEEEGK GILIIHSLFGPCSMSCSQNF SFL TDR R
857	6354	B	884	46	386	XIRHESGSRSHSHCSTLSSIGDVAKK LGEMWNNTAADDKQPYEKKAACL KEYYEKDIAAYRAKGKPDAAKKG VVKA EKSKKKKEEEEEDEEDEEDEE

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						EEEDXEDDDDEEEDDDDE*
858	6355	A	885	263	484	
859	6356	A	886	146	826	TWKGKDPKKPRGKMSSYAFFVQTC RGG\HKKKHPDASVNFS/ESFSKKCS ERWKTMSA*R/EKGKFEDMAKAD KARYEREMKTYIPPQRGRQKRKFK DSQLHPRGPPS\AFFPLLALEYRPKI K\GEHP\GL\SIGDVAKKLGRDVGIN TAAD\DKQPYEKK\AAKLKEKYEKD IAAYRAKGKPDAAKKGVVKAES KKKKEEEDEEEG\DEEDEEEDE EDEEDEEEDER
860	6357	A	887	1	456	RPRRPQREPTMVLSPADKTNVKAA WGKVGAGAHAGEYGAEALERMFL/SF PTTKTYFPHFDLSHGSSQVKGHGKK VADALTNAVGHVDDMPNALSALS DLHAHKL RVD PVNFKLLSHCLLV LAAHLP AEFTPAVHAFLDKFLASVS TVLTSKYR
861	6358	A	888	2	435	QTQREPTMVLSPADKTNVKA AWG KVGAGAHAGEYGAEALERMFLSFPTT KTYFPHFDLSHGSAQVKGHGKKVA DALTNV/EHVDDMPNALSALSDL HAHKL RVD PVNFQAPKATGLLVDP GPAHFPGRVSPRLRLQGLGTFKLG C
862	6359	A	889	9	390	NSARATDSERTHHGARLLPDKTNV KAAWGKVGAGAHAGEYGAEALERM FLSFPTTK\TYFPHFDLSHGSAQV GPTAKKVAERADQTPWRNVDDMP KRRCP*SDLH\AHKL RVD PVQLSS S*SHLPCW
863	6360	A	890	2	413	
864	6361	A	891	2	6281	
865	6362	B	892	79	200	XGDYPLGDLTPPTMEEATSGVNESE MAVASGHLNSTGVLE*
866	6363	B	893	209	502	MLLMYNSSDHDVYHMAVEMQRD VLEQIQFLATQLIMQTSESGISAKS LRGRDSTRKQDASEKDSVPMGSPA FFSLSLWDTSGFGWILNKIIPMTLS*
867	6364	A	894	283	340	
868	6365	B	895	1649	1741	MSFAMTLKKKLEEEAEVKKATD AA YQARQAVKTPPRRLPTVMVRSP DSASPGGDYPLGDLTPPTMEEATSG VTPGTLPSTPVTSPFGIPDTLP PGSAP LEAPMTPVTDDSPQKKMLGQKATP PPSPLLSELLKKGSLLPTSPRLVNE SEMAVASGHLNSTGVLEVGVLPM IHGGEIQTPNTVAASPAASESVSQ ATIVMMPALPAPSSAPAVSTTESVA PVSQPDNCVPM EAVGDPHTVTVSM DSSEISMIINSIKEECFRSGVAEAPVG SKAPSIDGKEELDLAEKMDIAVS YT AVEAALSFC EENDDPQSLPGPWEHP IQQERDKPVPLPAPEMTVKQERLDF EETENKGIHELVDIREPSAEIKVEPA EPEPVISGA EIVAGVVPATSM EPP EL

SEQ ID NO: of nucleotide sequence	SEQ ID NO: of peptide sequence	Method	SEQ ID NO: in USSN 09/770,160	Nucleotide location of first codon for peptide sequence	Nucleotide location of last codon for last amino acid of peptide sequence	Amino acid sequence (X=Unknown; *=Stop codon; /=possible nucleotide deletion; \=possible nucleotide insertion)
						RSQDLDEELGSTAAGEILEADVAIG KGDETPLTNVKTEASPESMLSPSHG SNPIEDPLEAETQHKFEMSDSLKEES GTIFGSQIKDAPGEDEEEDGVSEAA SLEEPKEEDQGEGYLSEMDNEPPVS ESDDGFSIHNATLQSHTLADSIPSSP ASSQFSVCSEDQEA IQAQKIWKKA I MLVWRAAANHRYANVFLQPGTR*
869	6366	A	896	3	2926	PGSTISSGTGKHKLLSTGPTWPWSIR EKLCLASSVMRSGDQNWVSVSRAI KPFAEPGRPPDWFSQKHCASQYSEL LETTETPK*VQSQRKRGEKGEVVE TVEDVIVRKLTAERVEELKKVIKET QERYR\RLKRDAELIQAGHMDSRL DELCN\DIATKKKLEEEAEVKRKA TDAAYQARQAVKTPPRRLPTVMVR SPIDSASPGGDYPLGDLTPTTMEEA TSGVTPGTLPSTPVTSPFGIPDTLPPG SAPLEAPMTPVTDDSPQKKMLGQK ATPPPSPLLSELLKKGSLLPTSPRLV NESEMAVASGHLNSTGVLLLEVGGV LPMIHGGEIQQTPTNTVAASPAASGA PTLSRLLEAGPTQFTTPLASFTN\VA S\KPPVKLVPPPVEFFSQATIVMMPA LPAPSSAPAVSTTESVAPESQPDNC VPMEAVGDPHTVTVSMDSEISMII NSIKEKCFRSGVTEAPVGSKAPSIDG KEELYLAEKMEIAVSYTGEELDFET VGDIIAIEDKVDDHPEVLDVA AVE AALSFCENDDPQSLPGPWEHPQQ ERDKPVPLPAPE\MTVKQERLDFEE TENKGIHELVDIREPSAEIKVEPAEP EPVISGAEIVAGVVPATS\MEPPELR SQDLDEELGSTAAGEIVEADVAIGK GDETPLTNVKTEASPESMLSPSHGS NPIDPLEAETQHKFEMSDSLKEES GTIFGSQIKDAPGEDEEEDGVSEAA SL*EPKEEDQGEGYLSEMDNEPPVS ESDDGFSIHNATLQSHTLADSIPSSP ASSQFSVCSEDQEA IQAQKIWKKA I MLVWRAAANHRYANVFLQ\PVT DIAPGYHSIVQRPMDLSTIKKNIENG LIRSTAEFQRDIMLMFQNAV MYNSS DHDVYHMAVEMQRDVLEQIQQLA ATQLIMQTS\ESGINAKSLRGRDS\T RKQDASEKDSVPMGSPAF\LLSLFD GGTQGTPLCPLKPDMMKKVKPQS YPL
870	6367	A	897	150	425	VYHFLVALKIPPSLMVFPCCPSPFPS/ PPRLPPHPVLFLPPSPSPSNP*VLGS PRGLSPPLL*GPP\PPKPACFCSP RDPGKLRWALRG
871	6368	A	898	65	259	
872	6369	A	899	273	962	KRERAVSLGQSGLPVVRAGPQGGG CTWGADALGGTGACGACSLRSSTP HFLGQSERVPH*QGG\TGIFHHPEHG S*AKK/DPVRPPCA*QGGKGAFLPA EA*VSGDQGGPGA VLS\GRDCPFPS

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						PGP/PGNPQPLAARQGPAPGNSGSL WPWQEPPVDWPSEGTP/GPLLRRQQL QSQPKNATGRERHPPQT/AKPFPSCP NTVL*IPEIK*NPWGEQQSRPALGST QDQRICNNH
873	6370	A	900	1	253	KRKVSLCHPGWSAGAPSRLTATSSS LV\KRFSCLSFPSWDYRCAPHLAN L/CRG/RGFTMLARLVLNS*PQMIYQ SRPPKVLGLQV
874	6371	A	901	327	638	LGLQGSTIFHKTLKKDLLQLEKQLN VNRDPGESNNSHNSQIKSFPKIYHFF FFGLLRN*PTNTLDRFVFGFENTHLS VL/QRKTISFNLVCWSHTPSINVCAI YQ
875	6372	A	902	834	1187	RKYETCLSALEIFT*SCSAVGII*FFC LFLGDEVLLCCPGLFTGCHHRWNY SLKLLGSKRSFCLSLSSWNYRHAP PSLGF*KNFKKNFE\KDLAML\PLGV FNS\YP*VILLWASSNG
876	6373	C	903	150	364	MSILPLQSYINMNAGNLYGQMHNH FPYIVKQKKQVCRTVCTVSLVYHK MCVYMCVCECLXXXXXXXXXXXXX X*
877	6374	A	904	29	372	SYENNHSYAGWSGSRKRFTLFLQIY /CRYITPLYILLYVFEQ*VYYPFKVT* I*MQEIYMDRCITIF/LYIVKQKKQV CRNSVYSITCLPQNVCGICVYVSVYI HTYIYIYTHHH
878	6375	A	905	1	815	MGNLGQVRRLSLWDYLLGLTHPRG LTTSQPGRSGLSPPAPPQQSFCMCQ NVTPGIMALGMSAVYFQVSGTKEQ PVPGHMPQSILLELWGFQVHHCV GNPRPDFMEHSKDLTSLLDHSHCH WHGRSHSSKEYLELHRENFLILRS AFPTGLLRAWPRDGISQYLLVELKN NMFRFLVAGSAEGAAGPPCPGPRK VAKKKPHLKQAPKNAGPRRWDEG R*GFPSQKQKEEQKKLGGA*KRKA RGGRGWPWTGGIK\KSGQKSKLFPW CLRRW
879	6376	A	910	140	512	PARGEGSRLDPSQWGEPAECAKEPT AVPRGPGLRNRTALTGTQKPPQSRE GARCIIGGSAPSTPPSSARRRWPGG HS*AGRPGRSSRQEPGCCIDRAPGP GLPPPASQPPGAAPLRCPTAVGPS
880	6377	A	911	68	675	RSTRTVHIPLLSCAQLPGQTP*PLSP WFFFCTPSSQGPEPREDQPGCAPG PQEAPKPAGNLPPTDSSARAASETG RVLPSP/PPTLIFCNLPRRG/FVSVAHL WLMSPFIRL*EATPGPGGQSGDLGG LILHPGQPGHGGQGGQGAAGALQR GP/DTSPTPCSRAAAAGMPTA*TLTP *RILPRTAPSPTTPGEQLPRPGNSGR DG
881	6378	A	912	3	3492	GGTVPQGLRTHGTGRGDTVGDGGE PPPQDRTLHLPQPPHPLPAPGQGA V PAGRGGGAAQP/AGSPTAPCGPGTS



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						GFAEDSREERGHRLPGEPEVPQP*R LHPG/PPGC/MPDVDFSNSFGESSDF DGLAGTSRN/RQAPGNPRSHGDIQA DRVPGWGHRRQAGGAEPGKGAEG GAAAAVPAAAGAPGPGRDPCRGA PAGG*PQPHEA*G*RTLP*GAEAEG RDAQPLAAL*QCAAGEGAGRLTLP QPAGGAVSTEAGAAASQHGFL* GIARAVPEDSQRPGVVRG*GAEPPEG GE*ETALADFQPGGEGHSGAEPGRG AGEPTGAGGAHPLAAGAGRGCREA ARAGQTLRAAELHGPCVPLCPVLG REGTDPAAPVEE*DGLPTLQGECE AAGPGVRAAEGARPGVLRGQCSE GDFPEPGGEGLPQAGVRADGPGL RAAHTASPAAGRASGCAQAG/RPGP GSPVHGRSSGWCGCMPSAPETTAT A\PRQLHRVSALVGPECHVQPRAGG QLPLQQPRAPQPAVPVQAGGRGLR GRTL VFQQLPGDPGGRPGSPAGS*G RRPTPGL*APRHGRPSAAGKQPAAS LPWKA*CLGECTSRSSPGLQRRPHA AEASPQDPEPGHHAGVPGGCIAGA DQHRHREPHGHLHPPGHPLGGGP DGLAPGHPCDG*LRLRALVQGS GGHDPGGGRGASQEGGRLLPVCE GQHGR*EATPGPGGQSGDLGGLIL HPGQPGHGGQQRGAAGALQRG AR/PPTPCSRAAAAGMPTA*TLTP*R ILPRTAPSTTPGLSSSS*PSSRT*LSS AP*PASHL/PGGPQ/IAGPHRQYQGS QGQPSAFVL*QGPVGPQQDGGQLQH VLLGRELPHPGALYPGAAPSTRPAP ACAPRAQGGWEDPERETVPPPRV*E VPGRVLEPGGV*GLEP\GGDIIPGGR GVRGPLLGEPA\SCGVPHGKEHPCP PGRPAGQCLHPAQDGHLPHRHPRL CQREDGKEAQEGPTAVGHLRGAAP GGCEAGGGRPGPGALSIQPPGS*RL ERPGRPAQLCPPGHRRRAEAGATPT SSKN*PQARGRASPPSNASVTEELT QGRGWALPPSNASVTEELTQARGR ASPPSNASVTEELTQARGRASPCLH LRRLSKKDKLLPRNTTGSKLITSGSL LPISWKPAWGTGT
882	6379	A	913	232	485	TRLRLTPKVCYPYRWSHFDRKFLSRV LMRRSAQKSRDRILNVFHELNL/NS VLDMRPMEF*GLRAAS*PQGERRGS LAFIREFHHT
883	6380	A	914	2	1163	
884	6381	A	915	771	1597	GACHLRLTPKVCYPYRWSHFDRKFP SARVL\MRRSAQKSS/RDRILNVFHE L\NLKDAISYVAEVAEPLALPGRGC SRLGHWLIQFWT*GQWSFRVSGLLP D/TQGERRGSLAFIRSPSTDNVNV DFTPRSSTVEASVSLLYVAMVMQ LPWGRAQPRELRVTDRAVVAPGLG VAWKRGEVQKEGVGVSSHKPSYIR

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						PWPDSLSAGRKVKGRGSSGLGARP DVFAPGPQQPVMVMPPLLLLRPW APQLTASSHRRSTLPDVQMLGSPSL TARALERDQ
885	6382	A	916	3	471	DSWLWWLRQRLQQIGGISGSTSTSS MLSRVCGTSRQLAPVLGYLGSRQ KHSLPDLPYDYGALPHINAQIMQL HHSKHHAAYVNNLNVT EEEKYQEA LAKGELLEAIKRDFGSFDKVKEL TAASVGGKGSCWGG LGFNKERGH LQIAAWPNQDP
886	6383	A	917	54	873	GPRAAQERHSLWWLRQRLQQIG GISGSTSTSSMLSRVCGTSRQLAP VLGYLGSRQKHSLPDLPYDYGAL EPHINAADHASLHHSKHHA/APYVN NLNV/TEEKYQGGGLWPRGDVYSPR* ALQPCT*KF\NGGGHIN\HSIF\WTN PQAPNGGGETQRGSLGSHQNVDF GS\FDKFK\EKLTAA SVGCPKAPGW GWLGFQ*GNRGH/LYQIAACPKSGI PLQGTG/LLFLLGIDVWEHALLPS SIKNVRPDYLKAIWNVINWENVTE RYMACKK
887	6384	A	918	24	452	APSPDAMG/HSLWGKVNVEDAGGE TLGRLLVVYPWTQRFFDSFGNLSA SAIMGNPKVKAHGKKVLTSLGDAI KHLDDLKGTFAQLSELHCDKLHVD PENFKLLGNVLT VLAIFGKEFTP EVQASWQKMVTGVASALSSRYH
888	6385	A	919	41	601	APSPRRPWGHFTEEDQGLLSTSLWG K\VKCGKNAGRKKPLGKAPLVVL/H PWDPKRSFEQALGNPVPLPSA\IMG NPPKSRAGK\KVLTS LGEMPIKHP G*SSKGTFAQA*SELHCDK\LVHDP ENFK\LLG\NVLT VLAIPFSAKEFT PGGCRASWAERWVTWSWPVPCSS RIPLSSLAHDCRAFQG
889	6386	A	920	14682	14931	EIGPGPRPLPSPLP*ATSTSVLAASGR PERTR/HAGIKIVLEDIFTLWRQVET KVRAKIRKMKVTTKVNRHDKINGK RKTAKEQSPLLQESLFATGDVSHNL LRALDVGLLANLSALAE DISNNKI STLEEGIFANLNLSEINLSGNPFEC DCGLAWLPRWAEQQVRVQPEA ATCAGPGSLAGQPLLGIPLLDSCG EEYVACL PDNSSGTVA AVSFSA AHE GLLQPEACSAFCFSTGQGLAALSEQ GWCLCGSAQPSSASFACLSLCSGPP PPPAPT CRGPTLLQHVFASP GATLL AAFHIAAPLPTATRWDFGDGSP EV DAAGPAASHRYVLPGRYHVM AVL ALGAGSALLGTDVQVEAAPAALEL VCPSSVQSDESLDLSIQNRVGSGL AAYSIVALGEEPARAVHPLCPDTEI FSGNGHCYRLVVEKAAWLQAQEQ CRAWAGATLAMVDSPAVQRFVLS RVTRSLDMWIGFSTVQGV EVG PAP QGEAFSLESCQNWLPGEHPATAEH

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						CVRLGPTGWCNTDLCALHSYVCE LRPGGPVQDAENLLVGAPSGDLQG PLMPLARQYGLSAPHEPVEVMVFP GLRLSREAFLLTAFTGTQELRRPAQ LRLQVYRLLSTAGTPENGSEPESSP DNRTQLAPACMPGGRWCPCANICL PLDASCHPRPAPMAARQGPGLLGA PYALWREFLFSVPAGPPAQYSVTLH GQDVLMLPGDLVGLQHDAGPGALP HCSPAPGHPGPQAPYLSANASSWLP HLPALQEGTWACPAALRLLAATE QLTVLLGLRPNPGLRLPGRYEVR VGNVSRHNLSCSFDVVSVPVAGLR VIYPAPRDGRLYVPTNGSASVLQVD SGASATATARWPGGSVSARFENAC PALVATFVPGCPWETNDTLFSVVAL PWLGEHEHVMVVDVENSASRANLS LRVTAEEPICGLRATPSPEARVLQG VPRYSPVVEAGSDMVFRWTINDK QSLTFQNVVFNVIYQSAAVFKLSLT ASNHVSNVTNVTNITVERMNRMQ GLRVSTVPAVLSPNATLALTAGVLV DSAVEVAFLWTFGDGEQALHQFQP PYNESFPVPDPSVAQVLVEHNVTH YAAPGEYVLTVLASNAFENRTQQV PVSVRASLPSEAVGVSDGVLVAGRP VTFYPHLLPSPGGVLYTWDFGDGSP VLTQSQAANHTYPSRGIYHVRLEV NNTVSGAAAQADVRVFEELRGLSV DMSLAVEQGAPVVVSAAVQTGDNI TWTFDMGDGTVLSGPEATVEHVYL RAQNCTVTVGAASPAHLARSLHV LVFVLEVLRVPAACIPTQPDARLT AYVTGNPARYLFDWTFGDGSSNTT MRGCPTVTHNFTSRGTFPLALVLSS RVNRARYFTSICVEPEVGNVTLQPE RQFVQLGDEARLVACAWPPFPYRY TWDFGTEEAVPARVGGPEVTFIYRD PGSYLVTVTASNNISAANDSALVEV QEPMLVTSIKVNGSLGLELHYLWD LGDGRLEGPEVTHAYNSTGDFTV RVAGCNEVSRSEAWLNVTVKRRVR GLIVNASCTVVPLNGSMSFSTSLEA GSDVRYSWVLCDRCTPISGAENEV GSAQDSIFVYVLQLEGLQVVGGR YFPTNHTVQLQAVVRDGTNIYSWT AWRDRGPALAGSGKGFSLTALEAG TYHVQLRATNMLGSAWADCTVDF VEPVGWLMVAASPNPAAVNTSVTL SAELAGGSGVVYTWSEGLSWET PEPFTTHSFPTPLHLVTMTAGNPL GSANATVEVDVQVPVSGLSIRASEP GGSFVAAGSSVPFWGQLATGTNVS WCWAVPGGSSKRGPHVTMVFPDA GTFNIRLNASNAVSVSATYNLTV EEPVGLVLWASSKVAPGQLVHF QILLAAGSAVTFRRQVGGASPEVLP GPRFSHSFPRIGDHVVSQSKNHVS

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						WAQAQVRIVVLEAVSGLQVPNCCE PGIAMGTERNFTARVQRGSRVAYA WYFSLQKVRGDSLFILSGRDVTYTP WPRGCWRSSSENRTLVLVQDAVQ YVALRSGPCFTNRLAQFEAATSPSP RRVAYHWDGFGDGPQDQTDKPR EHSYLRPGDYRVQVNASNLVSFFV AQATVTVQVLACREPEVDVVLPLQ VLMRRSQRNCLDAYVDLRDCVTY QTEYRWEVYRTASCQRPGCPARVA LPGVDVSRPQLVLPRLALPVGHYCF VFVVSFGDTPLARSIQANVTVAPER LVPITEGGSYRVWSDTQDLVLDGSE SYDPNLEDGDQTPLSFQWACVAST QREAGGCALNFGPRGSSTVTIPRER LAAGVEYTFSLTVWKAGRKEEATN QTCWWRPRALPSLFLMQILCNTTA CFSFASFQTCHSSTYSLQATYALVT KATQSPSNTNRSSWLQYTRHTHPVS SALCMPFRPGWKVANRMSILGGG WHDAEDAGAPLVYALLQRCQCG HCKEFCVYKSSLSGYGAVLPPGFRP HFEVGLAVVVQDQLGAAVVALNR SLAITLPEPNGSAMGLTVWLHRLTA SVLPGLLRQADPQHVEYSLALVTV LNEGPSRELVCRSCLKQTLHKLEA MMRILQAETTAGTVTPAIGDSILNI TGDLIHLASSDVRAQRSELGAESP LRMVASQAYNLTSALMRILTRSRV LNEEPAFSRAPANLSDVVQLVFLVD SNPFLFGYISNYTVSTKVASMAFQT QAGAQUIPIERLASERAITVKVPNSD WAARGHRSSANSVVVQPQASVGA VVTLDSSNPVAVLHLQLNYTLLDG RYLSEEPEPYLAVYLHSEPRPNERN CSASRRIRPESLQGADHRPYTFFISP GTRDPVGSYRLNLSSHFRWSALEVS VGLYTSLCQYFSEEDVVWRTEGLL PLEETSPRQAVCLTRHLTAFGASLF MPPSHVRFVFEPTADVNIYVMLTC AVCLVTYVMMAAILHKLDQLDASR GCAIPFCGQRGRFKYEILVKTGWGR GSGTTAHVGIMLYGVDSRSGHRHL DGDRAFHRNSLDIFQIATPHSLGSV WKIRVWHDNKGLSPAFLQHIIVR DLQTARSTFFLVNDWLSVETEANG GLVEKEVLAASHAALLRFRRLLVA ELQRGFFDKHIWLSIWDPRPSCFT RIQRATCCVLLICLFLGANAVWYG AVGDSAYSTGHVSRLSPLSVDTV VGLVSSVVVYPVYLAILFLFRMSRS KVLIDIDSLDSSVLDSSFLTFSGLHA EVRALLGVLGWAGGPAALALQLGL QTLCTSQQAFAGQVKSDLFLDDSK RSGPVVPVFPFPPCPKPPPLSWLPQG ALKGPGHAGIKIVLEIDFTLWRQVE TKVRAKIRKMKVTTKVNHRDKING KRKTAKEQ

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890	6387	B	921	1	714	MVKLSIVLTPRFLSHDQGQLTKELQ QHVKSVTCPCEYLRKVINTLADHR HRGTDFGGSPWLLIITVFLRSYKFAI SLCTSYLCVSFLKTIFPSQNGHDGST DVQQRARRSNRRRQEGIKIVLEDIF TLWRQVETKVRACKMKVTTKV NRHDKINGKRKTAKHELRKLSMKE REHGEKERQVSEAEENGKLDMEI HTYISPLLQESLFATGSEWRQRSIVI LQDCPTGPTSQLKL*
891	6388	B	922	1	387	MRVRWLLFWLLFWLLLGFIHQST CVINTLADHRHRGTDFGGSPWLLI TVFLRSYKFAISLCTSYLCVSFLKTIF PSQNGHDGSTDVQQRARRSNCRQ EGIKIVLEDIFTLWRQVETKVRAKIR KMK*
892	6389	A	923	277	489	
893	6390	A	924	465	634	
894	6391	A	925	1	4652	MGSTGVYKVTTPRSCHRFEQAFYTY DTSSPSILTLTAIRHHVLGTITDDKM MDVTVTIKSSIDSEPALVLGPKSV QELRREQQLAEIEARRQEREKNGNE EGEERMTKPPVQEMVDELQGPFSY DFSYWARVLCFVGTGPAKLKYINY FRSGEKITVTPSSKELLYPPSMEAV VSGESCPGKLIEIHGKAGLFLEGQIH PELEGVEIVISEKGASSPLITVFTDDK GAYSVGPLHSDLEYTVTSQKEGYV LTAVEGTIGDFKAYALAGVTLHSQ DVLMLPGDLVGLQHDAGPGALLHC SPAPGHPGPQAPYLSANASSWLPHL PAQLEGTWACPACALRLLAATEQL TVLLGLRPNPGLRLPGRYEVRAEVG NGVSRHNLSCSFDVVSPVAGLRVIY PAPRDGRLYVPTNGSASVLQVDSG ASATATARWPGGSVSARFENACPA LVATFVPSCPWETNDTLFSVVALP WLGEGEHVMDVVVENSASRANLS LRVTAEEPICGLRATPSPEARVLQG VPVVLLAGSSGYLVGFKFLESHGSD SGSANSFHRLISRNEFKTPLPDLTRV PRYSPVVEAGSDMVFRWTINDKQS LTFQNVVFNVIYQSAAVFKLSLTAS NHVSNVTVNYNITVERMNRMQGL RVSTVPAVLSPNATLALTAGVLVDS AVEVAFLWTFGDGEQALHQFQPPY NESFPVPDPSVAQVLVEHNVTHTY AAPAALGGGAVLTRQPSVLLHLC VPHVAWEPGLKAGPQVSTVLTVL ASNAFENRTQQVPVSVCASLPSVSV CASLTGACWYPRVLIRSGRPVIVSL ECVSCKAQAVYEVSRSYVYLEGR CLNCSSGSKRGGYTFTLTVLGRSGE EEGCASIPLSPNRPLGGSCRLDFPLG AVHALTTKVHFECMGWHDADAG APLVYALLLQRCRQGHCEEFVYK GSLSGYGAVLPPGFRPQFEVGLAVV VQDQLGAAVVALNRSIAITLPEPNG

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						SAMGLTVWLHGLTASVLPGLLRQA DPQLVIEYSLALVTVLNEYERALDV AAEPKHERQRRQAQIRKNITETLVSL RVHTVDDIQQIAAALAQCMRKLPE QDIAQGSYIALPLTLLVLLAGYNHD KLIPLLLQLTSRLQGVGALGQAASD NSGPEDAKRQAKKQKTRRTLATSIN TSREPSTDDQLPAHNQTMPQRHAR RSAPPRAYDRKTRQEENPHQTRSH AAAKRRERPPHDLQKQATTRLIPAG PRRRDGTSPRRTQPPNTRRPAAG HLARFRAAPGARGARPPTARRGR EELDPAHIYAAAPGLPTPPRAGRTPP TPERRDRNTRRRRTREEGEGEFPRV SFLKTIFPSQNGHDGSTDVQQRARR SNCRRQEGIKIVLEDIFTLWRQVET KVRAKIRKMKVTTKVNHRDKINGK RKTAKEHLRKL SMKEREHGEKERQ VSEAEENGKLD MN\*IHFYMEMFQR AQALRRRAEDYYRCKITPSARKPLC NRVSLLVFLAFGHSLPGQDMDTFFS LRLCASSPAEGDGREEGCLQAFVTP SLLVTVLRKNTFIPTQWGPHLIF
895	6392	A	926	3	156	EMFQRAQ/ALRRRAEDYYRCKITPS ARKLLCNRCTYNLVLPGSEKKYYSH A
896	6393	A	927	183	1518	ASTQSAVGLVSSVVVYPVYLAILFL FWMSRSKVAGSPSPTPAGQQVLDID SCLDSSVLDSSFLTFSGLHAEVINTL ADHQHRTDFGGSPSVLIITVSLRSY KFAISLCTSYLWVINTLADHRHRT DFGGSPWLLIITVFLRSYKFAISLCT TYLC\VSFLKTIFPSQNGHDGSTDVQ QRARRSNCRRQEGIKIVL\EDIFTLW RQVETKVRKIRKMKVTTK\ATRLT KIKERRKTAQDHWRL SMKEREHG EKERQVSEAEENGKLD MKEIHTYM EMF\QRAQALRRRAEDYYRCKITLF QRKPLCNVRMAAVEHRHSSGLPY WPYLP AETLKNRMGHQPPPTQQH SIIDNSLSLKT PSECLLTPLPSPALPS ADDNLKTPAECLLYPLPPSADDNLK TPPECLLTPLPSPAPP SADDNLKTPP ECVCSLPFHPQRMISRN
897	6394	A	928	123	1040	WRWFTIGTFRILLMFCCLGYEWSG /GCTTWHSAWV*GSSCHPAICFLCF VAKSDP*RNPGLRKERTPRSQQQG SWFGEDQKSGLSILWADIVHRT\DA FGGSPWLLIITVFLRSYKFAISLCTSY LCVSFLKTIFPSQNGHDGSTDVQQR AR\RSNRRRQEG LKSICMHTKKRVS SFAGIKIVLEDIFTLWRQVETKVR KIRKMKVTTKVNHRDKINGKKKTA KEHLRK\LG MKERE\HEEKERQVSE AEENGKLD MKEIHTYMEMFQRAQ ALRRRAEDY*QHDKITPSARKAFFA NRVQQWRQW
898	6395	A	929	39	525	TKFVLGTFQILFTASFHPSWWPLA